

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED BY

E. K. MARTIN, M.S.

AND

ALAN MONCRIEFF, M.D.

UNDER THE DIRECTION OF

THE EDITORIAL COMMITTEE

VOLUME THE THIRTIETH

SESSION 1936-37

PART II

MAY TO OCTOBER



LONDON

LONGMANS, GREEN & CO., LTD., PATERNOSTER ROW

1937

ALP

Section of Physical Medicine

President—GEOFFREY HOLMES, M.B.

[February 19, 1937]

DISCUSSION ON THE INDICATIONS FOR THE USE OF RADIO-ACTIVE THERMAL WATERS IN GREAT BRITAIN

Dr. C. W. Buckley: It may be admitted at the outset that the thermal effects on the system resulting from the use of water at various temperatures, and the mechanical action of douches, will be much the same whatever water is used, and that such simple procedures are productive of benefit when the water is drawn from the public mains. When, however, we come to deal with the more severe and chronic types of rheumatic disease, I am firmly convinced that the chemical action of the water used on and through the skin makes a material difference to the permanence of the relief—not to say cure—and in considering the indications for the use of the waters under discussion I shall try to avoid any effects which are not due to the chemical characters and are therefore common to all hydrological treatment.

It is a point of some interest in the argument that thermal and mechanical effects are not those of chief therapeutic importance, and that up to 1820 the Buxton radio-active water was only used in its natural flowing state at a temperature of 82° and without such mechanical aids as douches, so that the results obtained must have depended upon the chemical characters of the water. The reputation of the spa for the effective treatment of rheumatism and gout was made under these conditions, and the indications have not changed with the multiplication of methods.

There is one criterion of the chemical action involved in the external use of mineral waters of this type which deserves attention, namely the occurrence and degree of "bath reactions". Dr. Burt, in a communication to this section, has dealt very fully with this point and made it clear that very different effects result from baths of radio-active mineral waters as compared with those of plain water. He showed among other effects that an immersion bath at various temperatures between 80° and 100° caused a slight rise of temperature, but that this lasted for a much longer time with the mineral water than with tap-water, indicating a more profound effect upon metabolism. If anyone will try the effect of simple immersion in the Buxton natural pool for fifteen or twenty minutes and compare it with a similar time in an ordinary swimming bath he will easily be convinced of the difference; a disproportionate lassitude accompanied by muscular aches and pains is the usual effect, but if there is any tendency to gout this effect will be more marked and may culminate in an acute attack. A similar effect in the gouty sometimes follows much milder bathing unless regulated in details with the greatest care. As the patient is likely to have been in the habit of taking a daily warm bath at home, it is obvious that the chemical activity of the water is responsible for this effect, which is due to its action on metabolism.

It was formerly denied that the constituents of a mineral water could pass through the skin, but recent researches in France by Mougeot and others have shown that with gaseous waters osmosis undoubtedly takes place. In the case of the waters under discussion this is important, since the mineralization is too low for any

appreciable amount of the solid constituents to enter the system in this way, even if it could be demonstrated that such a passage could take place, but the gaseous content is high and strongly radio-active. Possibly there are other factors to be considered which are as yet unidentified, for a patient who was accustomed to go to Bad Gastein before the late War and had patronized many other continental spas, told me that he ranked Buxton, in respect of the potency of its waters, level with Gastein and far above Wildbad and the others with which he was acquainted. Any table of the relative radio-activities of the different springs will at once show that if this is the case some other factor must be taken into account.

Apart, however, from the entry of gases through the skin, which may have a local effect upon the subcutaneous tissues, they are absorbed in much greater quantity through the lungs. They are continuously given off from the surface of the water in which the patient is immersed, often up to his chin, and as they diffuse very slowly, the layer of air which he breathes is richly charged with the gases and the radium emanation. In baths which are artificially aerated this effect is enhanced by the action of the bubbles of air which, as they pass through the water, liberate the dissolved gases and emanation more freely and also bring them more forcibly into contact with the skin.

The internal use of the water brings into play other effects. It is strongly diuretic, the action in this respect being frequently impressed upon the notice of the patient in an unmistakable way, but an increased excretion of water, greater than can be accounted for by the increase in the quantity of fluid imbibed, will only continue a few days unless there has been an abnormal retention of water in the tissues previously. In a series of cases this effect was tested against that of similar quantities of distilled water and the mineral water was found to be much the more active. The elimination of sodium chloride was increased, but that of uric acid was decreased; this effect appeared to be due to more complete nitrogen metabolism, since it was accompanied by an increase in the urea excretion, the amount of total nitrogen excreted as urea being increased about 3% in the series of cases (16). At the same time, the hydrogen-ion concentration of the urine was reduced, that is, it became less acid, to a degree which could not be explained by the slight alkalinity of the water. Since it had been observed that the pH of the urine in gout cases admitted to the hospital was invariably excessive, this change appears to be of importance and is probably directly associated with more complete nitrogen metabolism. In a series of cases in which the blood uric acid was above normal, however, there was an increase in this respect at first, followed by a fall later, the explanation possibly being that uric acid deposited in the tissues was washed into the blood-stream and the level thus raised until the kidneys could eliminate it. It may be noted that simple warm baths also increase the elimination of sodium chloride, but I have no evidence to show that in this respect the effect of the radio-active water is greater than that of plain water.

In considering the indications for the use of these waters it seemed to me that it would be of interest to look up the work of Dr. John Jones who published in 1572 a book entitled "*The Benefit of the Baths of Buckstone*".

While some of the conditions that he enumerated are not sent to spas for treatment to-day, we may conclude that "weak sinews, cramps, numbness, and shrinkings, as well as rheumas" indicate various forms of fibrositis, sciatica, arthritis, and so on. That this was the chief type of sufferer who visited these spas at that time is confirmed by an Act of Parliament passed in the forty-third year of the reign of Queen Elizabeth the First, to regulate the passage of crippled persons to Bath and Buxton. They were flocking thither in such numbers in spite of the difficulties of travelling, as to throw a severe strain on the accommodation, and by reason of the poverty of many, upon the resources and benevolence of the inhabitants.

In 1697 Dr. Floyer published a book dealing with the waters of Buxton and the diseases treated there, and gives first place to gout, which no doubt may be accounted

for by the prominence given to this disease a few years earlier by Sydenham, who had differentiated it clearly from the general group of joint diseases and indicated its association with renal calculus and gravel, conditions also specified by Floyer as treated at Bath and Buxton with benefit. Floyer also lays stress on lameness and pains in the limbs, and scorbutic rheumatism, by which I think he means arthritis. This term is of interest, in view of the work of Rinehart, who has produced in animals a condition of the joints resembling arthritis, by withholding vitamin C from the diet.

To-day the benefit of treatment by radio-active waters and baths in rheumatic diseases and in gout is generally acknowledged, and these diseases remain the most prominent indications. Doubt is, however, often expressed as to the expediency of sending cases of rheumatoid arthritis in the more acute stages to a spa, but I believe that it is a perfectly sound procedure under proper conditions and far more likely to prove beneficial than being sent to the sea or any foreign resort. The craze for Algiers or Egypt in such cases has often done harm and there is little evidence that it ever did real good. Home treatment may be the best if it is adequate, but is apt to be depressing to a chronic invalid whose ailment is "only rheumatism" and who is encouraged to get up and about for fear of getting stiff—with disastrous results to the inflamed joints—or, if this is found impossible, is left to his or her own devices for hours at a time, the services of a nurse or masseuse to provide proper physical treatment being usually beyond the means of the middle-classes in these days of heavy taxation. A hospital, clinic, or nursing-home run on proper lines in a spa is likely to provide much more favourable conditions for recovery. It is important to recognize that even mild and ambulatory cases do better under such conditions, where diet is properly attended to and physiotherapy, including regulated rest, is part of the daily régime. In combination with such a régime I believe that the use of radio-active baths is of the greatest value and has some specific effect. Warm, but not hot, immersion baths, large and deep enough to permit of movements being freely carried out, are a characteristic feature of the treatment at the spas under discussion and therefore I do not hesitate to include rheumatoid arthritis at any stage as one of the most important indications for treatment by radio-active waters in Great Britain. Delayed convalescence and stiffness left after rheumatic fever are effectively treated along the same lines.

Fibrositis, including sciatica and brachial neuritis, is an important indication especially in cases due to toxic or infective causes, while those due to strain or other form of trauma are also likely to benefit, though in such conditions the radio-active element is of less importance and simple hydrotherapy may prove equally effective. Osteo-arthritis is another indication, though the possibilities of improvement will depend on the stage the case has reached and the extent to which fibrositis is associated with it, as pointed out by Gordon.

It is unnecessary to emphasize gout as the disease above all others which will be benefited by radio-active waters at any stage, both for prophylaxis and treatment.

In all these conditions there is a certain specific action, a "bath reaction" to which I have already referred. This is probably in the nature of a mild protein shock and needs to be carefully controlled.

I am aware of the negative results of radium emanation treatment in the valuable research recently carried out by Dr. Howitt and his colleagues at the Middlesex Hospital, but do not intend to discuss this in detail. It is a totally different thing from such a line of treatment as I have outlined, and in any case the activity of radio-active thermal waters, so far as they are found in Great Britain, is not due to radium only.

One of the indications given by Jones is of much interest, namely "heat and stoppage of veins"; clearly phlebitis, thrombosis, and varicose conditions are referred to, conditions which are treated with success both at Bath and Buxton,

though this is often forgotten in the popular craze for continental spas. Careful use of the radio-active immersion-baths allays inflammation, improves collateral circulation, and promotes the elimination of toxic products which are often an important aetiological factor.

Certain forms of hepatic disorder and catarrh of the colon due to residence in a hot climate—and often the sequel of dysentery—appear to do well. The line of treatment must necessarily vary with the type of case, but peat-packs made up with the mineral water and applied to the abdomen play an important part. Colon irrigation in moderation is often used in addition, the effect of the water when used for this purpose is, apart from the cleansing effect, sedative to the mucous membrane. Colitis of the simple catarrhal or mucous type, apart from tropical disorders, is also benefited by the same procedures, but the number and frequency of the douches should be strictly limited.

High blood-pressure of the type met with so often in women at the menopause is definitely benefited by these baths and the eliminative effects of a diuretic water especially in combination with douche massage and attention to the bowels, which often prove constipated to a remarkable degree even though, or perhaps because, aperients have been regularly used. Attention to the diet can often be secured and better habits in this direction promoted as a result of the course of treatment.

Other conditions are treated effectively by these mineral waters. Among these the signs of advancing age, the earlier stages of arteriosclerosis, &c. are important, as well as nervous and physical exhaustion from business strain, &c.

The radio-active thermal waters of Great Britain do not work miracles, and need as much care in prescribing them as does any other remedy.

F. G. Thomson: Since radio-active thermal waters have been systematically used in the treatment of disease, various theories have been evolved to explain their action. It would, however, obviously be a matter of extreme difficulty to determine whether their action is due to their physical properties, chemical composition, radio-activity, or a combination of all these factors. Clinically it is impossible to dissociate the effects which might be attributed to radio-activity, for instance, from the general effects of internal and external administration. Fortunately it is not necessary to demonstrate how and why any therapeutic agent exerts its effects before making the fullest use of it. The use of many valuable drugs is entirely empirical, and it must be admitted that the successful application of these waters is based rather on generations of clinical experience than on any more or less speculative pharmacological theories.

As the result of clinical experience extending over a good many years, I am inclined to say that these waters are specially useful in three classes of disorder.

(1) *Metabolic disorders* such as gout, obesity, mild glycosuria, early hyperpiesis, and the derangements incidental to the menopause. These waters have been so closely identified with the treatment of rheumatic diseases, that their value in metabolic disorders, due rather to dysfunction than to organic disease, is apt to be overlooked. Whether the good results are obtained by means of diuresis, sweating, metabolic stimulation by heat, radio-activity, or a combination of these, it is impossible to say. In many cases of gout care is essential in prescribing even the mildest form of bath treatment, for fear of exciting excessive reaction. In obesity and climacteric disorders one can safely and with advantage apply more vigorous measures, including douches, massage, and so forth, combined with water-drinking, to carry off "fatigue products" and metabolic waste products. The relief of so-called hepatic glycosuria is often very striking and suggests that dysfunction of the liver, and possibly also of the pancreas, may be a more important factor in such cases than we are apt to think.

(2) *Rheumatic diseases.*—Patients suffering from chronic rheumatic diseases have always formed a large proportion of the cases coming for treatment to spas possessing

these radio-active waters. I am inclined to think that the good results obtained are due not only to the specific action of the waters but also to the particular methods commonly used. Owing to the large quantity of the natural water available, and its suitability for this form of treatment, the deep pool bath with hot undercurrent douche has always been the most important feature of treatment at these places, and I am convinced that, taking it all round, this particular type of bath is of more value in chronic rheumatic diseases than any other. The general effect of sub-thermal immersion on the circulation and metabolism, together with the local effects, either sedative or stimulating according to the pressure applied, of the undercurrent douche, renders this form of treatment peculiarly suitable for the majority of cases of rheumatoid or osteo-arthritis, together with lumbago, sciatica, and other types of general fibrositis.

In acute cases, not only of rheumatoid arthritis but of lumbago, sciatica, or osteo-arthritis, in which severe pain is a prominent feature, treatment can only be of the most gentle description to avoid excessive reactions and more pain, and unless special precautions can be taken to minimize the effort and fatigue entailed in taking a course of baths, it is better to defer treatment till the acute stage has passed.

In the treatment of osteo-arthritis one cannot, of course, expect more than relief of pain and possibly some arrest of the inflammatory processes in the affected joints, and here, again, the deep immersion bath with local hot douche appears to be by far the most effective form of treatment. In the more chronic stages of osteo-arthritis, and in chronic fibrositis, the deep bath may with advantage be combined with—or replaced by—the massage douche bath.

(3) *Diseases of the urinary tract.*—Owing to their powerful diuretic effects, radio-active thermal waters, combined if necessary with urinary antiseptics or other suitable drugs, are definitely useful in catarrhal conditions of the renal pelvis or bladder, whether due to *Bacillus coli* or other infection, or to uric acid or oxalic crystals. In the case of uric acid they appear to have some action, not only in causing the physical removal of small deposits of biurates, but also in preventing their formation by causing uric acid to be excreted in more soluble combination. The use of diuretic waters in the treatment of urinary disorders has received little attention in this country, and they might with advantage be applied more widely than they are now.

Professor Sidney Russ: Spa waters often contain radium or radon or both, but it is equally true to say that practically every river, lake, and ocean in the world also contains these elements. For some reason, however, which I have always found it very difficult to understand, this existence of minute traces (they are always exceedingly minute) of radium or radon in the spa waters has been put forward as a reason for some of the therapeutic value of the drinking water of the spa.

If it were so, it might be expected that the spa waters richest in these elements would be among the most noted. This is far from the case. One need do no more than cite the case of Sweden. Sweden has many spas, but the healing properties of these spas can scarcely be connected with their radio-activity, for the drinking-water of Stockholm from the artesian borings in the granite is far more radio-active than that of any one of the spas. If indeed the curative value of spa waters were due to their radio-activity, their value as health resorts might disappear very easily, for radium or radon impregnated water can be made at trifling cost. For instance, to obtain 9 mache units per litre, i.e. rather more than the strength of Buxton natural spring gas, and using $2\frac{1}{2}$ million litres daily, the quantity of radium necessary to activate it would cost about £200.

It is sometimes said that small quantities of radium invigorate the body. This is rather a loose term, but let us see to what extent it is likely to be the case. One approach to the subject would be from an energy standpoint.

1 gram of radium emits 134 cal. per hour I
 The average man's requirements are (according to Prof. Samson Wright)
 1.2×10^3 cal. per hour II
 Assuming that man could safely tolerate $\frac{1}{100}$ mgm. in his body, continuously acting (this is very doubtful, bearing in mind the New Jersey dial-painting tragedy), the energy liberated from this would be 134×10^{-5} cal. per hour, and would contribute about one-millionth of the heat requirements of the body.

It has been said that the rationale of the radium treatment of rheumatism is one of oxidation and de-toxication. We have for the last two years been carrying out some experimental work on the oxidation which can be produced by beta radiation, and I will quote from one experimental result which Mr. Spicer of the Radon Centre, at the Middlesex Hospital, has recently obtained. A typical oxidation process is the production of hydrogen peroxide from acidulated water. This can be brought about by beta radiation. Pure water acidulated with sulphuric acid has been exposed to beta radiation from quantities of radon with the following result:—

A concentration maintained at 9 mache units per litre would produce about one thousand-millionth of hydrogen peroxide per day.

A thousand-millionth of a milligramme of hydrogen peroxide formed in the body per day is an exceedingly small quantity, but I must leave it to others to form their own opinion as to what possible effect it could have upon the metabolic processes of the body.

Finally, I might refer to some clinical work in which I have been associated with Dr. Frank Howitt during the last four years. The object of this work has been, in the first instance, to determine what physiological and biochemical changes might be produced in patients by ordinary tap-water containing measured quantities of radon.

In a paper on this subject, which is just completed, Dr. Howitt has been forced to the conclusion that in the systematic treatment of cases of rheumatism and allied affections no demonstrable change was found in their clinical condition during treatment and that patients seen two years after treatment did not ascribe any permanent amelioration of symptoms to the treatment.

When we consider the great benefit that patients derive at spas, due no doubt to the medical advice they receive, the régime of life they follow, the drinking of waters containing a considerable variety of chemical compounds which can reasonably be held to have some definite action upon the body processes, it seems to me a pity to drag in radio-activity. I would go further and say that medical men, especially those in charge of important spas, would be doing a service if they rejected the claim; it leads to exploitation by the non-medical, and I have on more than one occasion tried to protect the public from being exploited in this way.

Dr. Frank Howitt: No one can deny the value of spa treatment; indeed we all have patients who can testify to this. With regard to the ingestion of natural waters, it requires a very small knowledge of physiology to realize that the contents of these spa waters may alter considerably the osmotic pressure, the pH value of the blood, and the activation of the endocrine glands, and may produce many effects as yet unknown. Possibly the waters of certain spas contain minerals and other ingredients in exactly the correct ratio to correct the defects of certain chronic pathological conditions resulting from metabolic disturbances.

I am no authority on these subjects, and the only point on which I wish to touch is the ingestion of ordinary radon in simple tap-water. I have recently carried out some work with Professor Russ and Dr. Pillman-Williams in this connexion, and the gist of our results has been given in Professor Russ's preceding remarks. Our observations were confined to two classes of cases—out-patients and in-patients.

In the former we gave radon water in dosages such as those obtainable from the apparatus which have appeared on the market. In the latter we pushed up the dosage, under full observation, until evidence of systemic damage was obtained.

The clinical results of these experiments were as follows: In dosages such as those obtainable from apparatus in present use, no demonstrable change was found in the clinical condition. Subjective improvement, due to the psychological stimulus and to other factors operating during the experiment, was neither more marked nor more frequent than in the controls. Patients seen two years after treatment did not ascribe any permanent amelioration of symptoms to the treatment. On the other hand, the blood-counts were not affected, and no injurious results were encountered.

In the series of cases (in-patients) in which radon was given in very much larger doses, no improvement was noted in the clinical condition except in certain cases of chronic gout. The chemical analyses of the blood were unaffected, again with the exception of the uric acid readings in this latter group. The erythrocyte count, however, showed a tendency to fall when large doses were employed, in certain instances to a serious degree. It appears, therefore, that with large dosage the administration of radon is attended by definite risk, and it should be administered with great caution.

I wish to emphasize, however, that these observations have nothing to do with spa waters, in which the mineral content must play an important part.

The President said that his early experiences in balneology had firmly convinced him of the value of radio-active waters. Shortly after qualifying and holding the usual resident appointments, he had acted as "locum" in a well-known hydro. There he was frankly astonished at the good therapeutic effects of tap-water applied in accordance with the principles of hydrotherapy and without the use of any drugs. Shortly afterwards he had held the appointment of house-physician at the Devonshire Hospital, Buxton. A few days after beginning his duties he had taken a prolonged swim in the natural thermal swimming bath, and had experienced a typical bath reaction totally different from the effects of a swim of the same duration in an ordinary swimming bath. During his time at the hospital and during two years spent in private practice in Buxton he had had ample opportunities of observing these bath reactions in rheumatic and gouty patients, and they had differed not only from the effects of the application of plain water, but also from the effects of the Harrogate sulphur waters in the use of which he had now had considerable experience. This was not the time for a discussion of the comparative merits of radio-active waters and sulphur waters, but he was convinced from personal observation, of the effect of both these types of waters, that they had definite therapeutic value and produced some effects not obtainable by the use of plain tap-water.

Dr. J. Barnes Burt: The papers by Dr. Howitt and Professor Russ should be of great help to those physicians who practice in spas. They show convincingly that in rheumatoid arthritis the internal use of water impregnated with radon has very much the same action as tap-water when taken by the mouth, though in gout the internal use of radon does appear to have brought about some improvement.

In spas, however, the conditions are totally different, for it is by bathing in radio-active water, and not by drinking, that we obtain most of the beneficial results. It is to be remembered that the strength of radio-active waters is always spoken of in terms of the alpha-ray activity. A natural spa-water that contains radium emanation must also contain the disintegration products of radon, down at least to radium D. The water therefore as it rises from the spring must contain a mixture of alpha, beta, and gamma rays.

It is possible that the penetration of the skin at different depths by alpha, beta, and gamma rays, explains the therapeutic action. Baths have the advantage of

bringing the skin into direct contact with these rays and in running water fresh rays are continually carried to the surface of the whole body, so that in spite of the weakness of the radio-activity of most spa waters, a considerable dose of rays is absorbed in the ten minutes which clinical experience has found to be the best average period for natural baths.

Dr. L. C. Hill said that in endeavouring to assess the value of radio-active waters it was a little difficult to exclude such factors as the bracing and stimulating effect of a change of climate, temporary freedom from domestic cares, and a more regular regimen. It seemed to him that the whole question of whether special effects were produced by immersion in radio-active water as compared with tap-water, depended upon the belief in the existence of bath reaction (thermal bath crisis) and bath or thermal debility. The former occurred commonly during the first and second week of treatment and consisted of an exacerbation of joint-pains, with lassitude and depression, while the latter was the somewhat clumsy title coined to describe the condition of fatigue, lassitude, and weakness, which followed a course of mineral water baths and was possibly a reproach to the physician in charge, indicating too long a course of baths or too many on consecutive days.

Some time ago he had spent some uncomfortable weeks in wading through a portion of the immense amount of pseudo-scientific continental literature on the subject, and as a result had no hesitation in condemning the vast majority of the experiments described as valueless, the evidence being based upon nebulous and unscientific data.

One experiment, however, which did appear to be based upon more reliable data, was that carried out by Dr. Fritz of Wildbad: One of the main difficulties of research in this branch of therapeutics lay in the procuring of satisfactory controls, because patients naturally came to a spa with the definite object of undergoing a course of mineral water treatment and were not easily satisfied with the alternative of tap-water. Owing to a spell of icy weather, the supply of mineral water was suddenly cut off, and those rheumatic patients who were at the moment undergoing treatment, continued to receive their baths at the hands of the regular bath attendants, but the town supply was laid on instead of the radio-active mineral water. While the attendants and nurses were in the secret, the patients were throughout under the impression that they were bathing in radio-active spa water. Of the twenty or more patients, each of whom had twelve tap-water baths, only one complained to Dr. Fritz of symptoms of bath reaction, while later, when a break in the weather occurred and it was possible to give the same number of patients an exactly similar number of mineral-water baths at the same temperature, only three failed to exhibit typical symptoms of bath reaction, and they all spontaneously remarked upon the difference in the effects of the two courses.

Section of Epidemiology and State Medicine

President—Surgeon Rear-Admiral SHELDON F. DUDLEY, O.B.E., R.N.

[March 12, 1937]

THE EPIDEMIOLOGY OF ANIMAL AND HUMAN DISEASES

By Sir FREDERICK HOBDAY, C.M.G., F.R.C.V.S., F.R.S.E.,

Dr. Med. Vet. (h.c.) Zurich

THERE are certain diseases of animals and man which are of mutual interest to the medical man and the veterinarian, either on account of their analogies or their differences, or by reason of the fact that they are contagious from animals to man or vice versa, and it is not wise for either branch of medicine, nor yet for our mutual patients, for us to work in watertight compartments. It is better from every point of view that we work in collaboration. Some diseases, such as cancer, tuberculosis, anthrax, and tetanus, we attack respectively in somewhat different ways; whilst others, such as glanders, rabies, foot-and-mouth disease, mange, and ringworm, can only be effectively dealt with by definite collaboration between medical men and veterinarians. There are others in which as yet there has been no effectual attempt at collaboration. Such ailments as common catarrh and the influenzas can be dealt with to mutual advantage from a comparative aspect, as can more complicated ailments such as Hodgkin's disease, and such common ailments as rheumatism and fibrositis. An exchange of ideas as to the symptoms, methods of spread, &c., in our various patients is of undoubted help towards elucidation. In veterinary medicine, equally with the human side, the study of collateral branches of science, such as entomology or parasitology, is of material help, and in teaching colleges, as in hospitals, a knowledge of the life-histories of the various flies and insects which act as carriers or transmitters of parasites is as essential to the veterinary student as to his medical *compère*. In the clinical world too, we have many points in common, for our animal patients suffer from gastritis, indigestion, colic, internal parasites, colitis, swallowing of foreign bodies, and various forms of pneumonia and heart

disease, to the same extent as human patients do, and our veterinary treatments are similar in principle to those in human practice. The veterinarian has, however, a greater variety of internal arrangements to deal with, having to take into account whether his patient is herbivorous or carnivorous; or whether, as is the case in man, it will eat anything and everything which it has an opportunity of eating. Some of our patients have only one stomach, whereas others have four—while the camel stands by itself in having three—so that their respective digestive processes vary very much in detail.

The veterinarian has, however, one advantage, at all events, over his medical *confrère*, in that when his patient becomes hopeless or in such pain that it is unkind for it to be kept alive, he can always administer euthanasia—and much pioneer work has been done here by the veterinarian which may some day usefully come into the realm of human medicine.

I feel sure that when a number of these diseases, both epidemic and otherwise, are studied from this point of view, we shall be able to advance more quickly and find many new ideas and theories, which up to the present have not been thought of. It is not only in Great Britain that diseases may be studied in this way, for those who live in the tropics have also plenty of opportunity for following up comparative medicine. The different effects which various foods have on man and animals also form a good illustration. For example, the flour of certain forms of Indian pea has a nerve-paralysing effect not only on the natives continually fed on it but also on horses, producing laryngeal paralysis which causes dyspnoea on the slightest exertion. Again in entomology, in the study of the life-histories of the various flies and insects which act as carriers and transmitters of disease-germs or blood-parasites, the knowledge acquired by collaboration is of mutual benefit in epidemiology, not only in the diseases transmitted from animal to animal but in those transmitted from animal to man. In the short time now at my disposal I shall confine myself to a selection of a few diseases which I think most likely to interest those who are especially concerned with Public Health, as being diseases which are communicable to man, and in the treatment of which the practitioner of human medicine can obtain material help from collaboration with his veterinary *confrère*.

Glanders.

This is primarily a disease of the horse tribe, and affects horses, asses, and mules. Its cause—the *Bacillus mallei*—is an extremely dangerous organism to work with in the laboratory. The disease is one which is most commonly met with amongst stable-workers and those who come in contact with horses, and some twenty years ago grooms and stablemen of studs in our big cities all knew its name. A man can be readily infected by the discharge from the nostrils of an infected horse or even by handling the brushes, sponges, or stable-cloths, which have been in contact with a glandered horse. In the South African war it accounted for the deaths of many thousands of our Army horses, and indeed in all wars it has been the bugbear for which the army veterinary officer must always be on the look-out.

Horses suffering from this complaint are unable to do their work properly, and it is so insidious that, until it has been present in the system for a certain length of time, its presence may remain unsuspected. Modern veterinary science has now, however, at its command a method by which the presence of glanders can be ascertained, for by the introduction of a few drops of mallein (a special preparation made from the *Bacillus mallei* itself) the skilled veterinarian can make a diagnosis with certainty within forty-eight hours, even if the animal is infected only in the slightest degree. During the Great War, by means of this test, applied by the officers of the Royal Army Veterinary Corps, glanders was entirely eradicated from the horses and mules

of the British Army, and it has been applied so successfully in Great Britain that at the present time the disease has absolutely ceased to exist. This means that now it has been eliminated from the list of ailments which the veterinary surgeon is called upon to diagnose; it has also been eliminated from the list of diseases in man, and so long as the present regulations of the Veterinary Department of the Ministry of Agriculture and Fisheries are kept in operation, man and animals in this country will be unassailed by this terrible affection.

Rabies.

This disease has not been met with in man in England for more than thirty years, and it can never appear again as an epidemic in this country, so long as control is kept upon the importation of animals of the dog and cat tribe. The primary cause of rabies in man is the contact of an abraded surface of the body with the saliva of a rabid animal, and whether the infected animal is a horse, a sheep, or any other animal, it has always had its primary origin in a rabid dog or cat. The Muzzling Order, which was imposed a number of years ago, succeeded in eradicating the disease from Great Britain, and it then remained for the Veterinary Advisors to the Ministry of Agriculture and Fisheries to take steps to see that it was not reintroduced into the country. This explains the present quarantine regulations imposed on all dogs and cats admitted from countries where rabies exist. The decline in the incidence of the disease is further proof of the value of the collaboration between the forces of the veterinarian and the medical man in the cause of Public Health.

Anthrax.

This condition is particularly met with in cattle, horses, sheep, and pigs; the dog, cat, and fowl possess a comparatively high power of resistance to the infection. It is a disease which is always serious and, in animals, invariably results in death. In cattle, especially, death is very sudden, and the Government has imposed laws and regulations which provide that the body must be cremated as near as possible to the place where the animal died. It is forbidden too, in any way to cut the carcass, for on many occasions those making, or assisting at, the post-mortem have become infected and have died in consequence. In Liverpool, Bradford, and other districts where wool from foreign countries is handled, disinfection is compulsorily adopted, with satisfactory results. If this practice could also be efficiently adopted in the case of hides, bone manure, and other animal products, before they are imported into this country, the number of deaths from anthrax in man and animal would diminish considerably. Cotton, linseed, and other cattle-food cakes, come into the same category. Once eradicate anthrax from the animal and animal products, and eradication from man would automatically follow. Anthrax is primarily a disease to be dealt with by the veterinary surgeon.

Foot-and-mouth Disease.

This disease, so much to the fore at the present time, has in the daily Press provoked a good deal of unwarranted criticism directed against the Veterinary Advisors to the Ministry of Agriculture and Fisheries, yet there is no doubt that they have adhered to the correct policy (that of "stamping out"). We have much upon which to congratulate ourselves when we compare our position with that of other European countries. The cost to Holland, France, Belgium, Denmark, and Germany, amounts to tremendous sums each year, and these countries never get any further forward in the matter, having the disease always endemic.

The following statistical table, showing the respective numbers of outbreaks in other European countries during 1934, is convincing evidence :—

Month	Great Britain	France	Germany	Holland	Belgium
January	1	1,074	113	579	329
February	—	652	80	214	168
March	—	613	73	105	102
April	—	287	110	59	81
May	1	135	48	51	40
June	—	146	66	132	36
July	—	98	27	459	19
August	3	92	40	1,391	15
September	4	21	19	3,120	90
October	24	15	14	2,880	9
November	28	3	16	48	1,173
December	18	28	32	230	20

The public should think what a terrible disaster it would mean to England if the disease were allowed to spread, with the fact before it that milk from cattle affected with foot-and-mouth disease must not on any account be consumed by children or invalids, or be given to goats, pigs, or any other animal.

Tuberculosis.

This is pre-eminently a disease which illustrates the value of collaboration between the medical man and the veterinarian in the cause of Public Health. No variety of domesticated animal is immune to tuberculosis, although some are more susceptible than others. The goat, the sheep, and the horse, are probably the least affected, but even in these it is only a question of degree, and there is no actual immunity when they are placed under conditions favourable for infection. Birds, especially poultry, are frequently affected, and whenever the disease appears amongst them the whole flock may have to be destroyed before it is eradicated.

It is a disease which the practising veterinarian meets with most commonly in cattle, and there are about a million tuberculous cattle in Great Britain at the present time. These are not all dairy cattle, but it is in these that the danger lies for man, as it is well known that at least 40%—and, in some districts, 60%—of them are affected.

It has been estimated by a late medical officer for the City of London that out of fifty consecutive samples of milk which had been purchased within the city boundary, not less than one in four proved to be tuberculous; and at one of the National Milk Conferences Dr. Stanley Griffith, in a paper on "Bovine tuberculosis and its relation to man", gave some statistics which went to prove more than ever the necessity for medical practitioners and veterinarians to pull together. In an investigation of 1,200 cases of tuberculosis he had found that 87·5% of infections with tuberculosis of the cervical glands, in children up to the age of 5, were bovine; and similarly 61·3% of those between 5 and 10 years; 37·9% of those between 10 and 16 years; and 25% of those of 16 years and over. Of 476 cases of bone-and-joint tuberculosis 28·7% of those under 5 years were of bovine origin; 23·1% of those between 5 and 10 years; 9·5% of those between 10 and 16 years; and 6·4% of those of 16 years and over. Of 126 cases of lupus: 69% of those under 5 years; 42·5% of those between 5 and 10 years; 60% of those between 10 and 16 years; and 17·6% of those of 16 years and over were of bovine origin. Similar percentages were found in connection with other diseases, and of 113 post-mortem examinations conducted by the Local Government Board, it was found that in 21·3% of those under 5 years at death, the infecting organism was bovine, and similarly in 13·4% of deaths between 5 and 12 years. The same medical scientist estimates that tuberculosis contracted through the consumption of cow's milk causes approximately 3,000

deaths in young children every year. As all these infections are caused by drinking the milk of cows suffering from tuberculosis of the milk glands, it is hoped that the new regulations now in operation—compelling the owner of a cow presenting any symptoms suspicious of tuberculosis to call in a veterinary surgeon—will have the effect of eliminating, in a great measure, the chances of infection from the cow to man.

That this state of affairs exists in such an enlightened country as Great Britain to-day does not speak well for its dairy cattle hygiene, and makes one wonder how any milk-drinking infants can escape infection. However, only about 1% of dairy cattle is affected in the udder, and until the infection has reached this organ the milk does not necessarily contain tubercle bacilli. At the same time an infected cow is always a possible source of danger, for one can never tell exactly when the udder tissues will become infected and the milk a source of definite and terrible danger to the children to whom it is given.

Pasteurization, undoubtedly, offers some safeguard, but it is generally admitted that some of the valuable properties which raw milk possesses are lost during this process, and there can be no doubt that the best solution of the prevention of infection lies in the endeavour to obtain an absence of the tubercle bacilli at the source of supply—i.e. the dairy herd. That this can be accomplished, if pecuniary and other necessary adjuncts are available, has been proved by actual experiments, and America has been especially go-ahead in her endeavours to form accredited herds. In that country whole districts have been cleared, and the most stringent laws are enforced in order to prevent reinfection by the entrance of tuberculous beasts into these areas.

In Great Britain progress in this direction has been slow, as the British public, although not unmindful of the advantages of tuberculosis-free milk, is not willing, as a body, to pay an extra price for this guarantee. Dairymen who have gone to the expense and trouble of clearing their herds have not received the encouragement they deserve either from the general public or from the hospitals and medical practitioners. These last, in particular, might do a very great deal more than they are doing to assist in educating the housewives and mothers of young children as to the dangers of tuberculous milk, by urging upon them the necessity for demanding a clean milk supply, i.e. one from tuberculin-tested cows.

This matter is now being seriously taken in hand, and a Veterinary State Service is being formed, with a staff of whole-time men whose duties consist mainly of inspection of dairy cattle with a view to the formation of tuberculosis-free herds. A clinical inspection is made of the udders periodically, usually four times a year, and for the owner who wishes to ensure that his herd is completely free from tuberculosis the cows are tested with tuberculin—of which we now have a synthetic variety—and by the intradermal method which forms a much more delicate test than the former subcutaneous method. We have reason to hope that this newly formed Veterinary State Service is thoroughly justifying its existence and that it will prove of benefit not only to human beings, by getting rid of a source of tuberculous milk, but also to the dairymen and the agriculturist, by weeding out from his herds tuberculous cattle whose presence is always a source of danger. It is a common observation that the herds from which tuberculosis has been eliminated are much more resistant to other ailments—the services of the veterinary surgeon being less in demand than when this disease existed.

Mange

Mange of the horse is now dealt with in all parts of Great Britain and is compulsorily notifiable under a Mange Order issued from the Ministry of Agriculture and Fisheries. Its spread has been effectually checked, and although it is not yet

completely eradicated, the number of cases in the horse is now extraordinarily small. It is, however, to the domestic pets, especially the dog and the cat, that attention should be drawn, for it is quite an easy matter for a pet dog to transmit the parasite of mange from itself to its owner. An itchy dog should, therefore, always be regarded with suspicion, and the pernicious habit of allowing a dog to sleep in bed with a human being should be emphatically discouraged. A dog with mange, especially in hot weather, or when its body becomes heated by lying in front of the fire (or sleeping on an eiderdown or blanket), will be continually scratching, especially in the region of the armpits and under the thighs, where the body is hot and the hair is thin. If no treatment is adopted, the dog will break out in sores, the hair will fall off, and the animal will presently smell very offensively and become covered with scabs. If allowed to come into contact with any part of the human body for more than a few minutes, it is quite an easy matter for the parasite to transfer itself to its human host, and it may remain for a considerable number of days, or even weeks, until it has finished its life-history. During this time it will give rise to a great deal of irritation and discomfort, which could easily have been prevented had the owner of the dog sought veterinary advice.

There are numbers of other diseases in which it is of value to the public health service that in the fight for their eradication the human physician and the veterinarian should collaborate, for the patients of each are equally attacked. Cancer may be taken as a type. This dreaded disease is recognized in such veterinary patients as horses, cattle, dogs, cats, and even in fish, and many of the theories which research-workers form, if their observations are concentrated on man alone, may at once be seen to be erroneous upon comparing notes with veterinary pathologists, whose lives bring them in contact with the comparative aspect. In foreign countries this has for a long time been recognized, and their governments have granted liberal funds for research into the problems of animal diseases and their relation to public health, finding it a paying proposition—even if considered only from the economic standpoint. Great Britain has been behindhand in this respect, but during the past few years with the establishment of the Animal Research Institute connected with the Royal Veterinary College at Camden Town and of the Institute of Animal Pathology at Cambridge, together with the creation of University Veterinary degrees and a Post-Graduate Diploma of Veterinary State Medicine, there is a good prospect that, long before another decade has passed the Government organization of Veterinary Officers of Health will have as important a place in Public Health as is accorded to the graduates of the human branch of State Medicine.

As I explained at the beginning of my paper, my list of those diseases which may furnish valuable instruction in the epidemiology of animals and man is by no means complete, but I must in conclusion mention one other—namely contagious abortion of cattle, in its relation to undulant fever of man. Sir Weldon Dalrymple-Champneys has for several years made a special study of this disease—of which I only know from what I have read—and I will leave him to deal with it in the discussion.

Discussion.—Sir WELDON DALRYMPLE-CHAMPNEYS, opening the discussion, referred to some of the interesting and difficult problems in connection with the transmission of Brucella infections. Contagious abortion of cattle was, he pointed out, a very infectious disease, easily transmitted from animal to animal, yet he knew of no well-authenticated case of man-to-man transmission of undulant fever, of bovine, caprine, or ovine origin, in the long history of this disease. The comparative immunity of veterinarians from the clinical disease was also puzzling when one considered how frequently many veterinary practitioners plunged their arm, almost to the shoulder, into the uterus of an infected cow in the process of "cleansing," i.e. delivering the after-birth. This procedure quite often resulted in the development of a specific skin rash on the arm but apparently was very seldom followed by a clinical illness (there were only four cases in veterinarians in his, the speaker's, series),

and at the Annual Congress of the National Veterinary Medical Association at Folkestone in 1932, agglutination tests on the blood of 63 volunteers who had come into close contact with infected cattle had resulted in only 15 positive reactions to a titre of 1 : 20 or over with an average titre of less than 1 : 60, whereas the average titre in his (Sir Weldon's) series of about 360 clinical English and Welsh cases was about 1 : 1,500. He had lately received an inquiry with regard to the possibility of undulant fever being conveyed to man by uncooked vegetables contaminated by the manure of infected animals, but he knew of no record of such an occurrence, though a small epidemic of the disease in France had been traced to the handling of the manure of infected goats.

Turning to rabies, he would like to ask Sir Frederick whether European bats had ever been suspected of conveying this disease in the same way as vampire bats had been shown to have done in Trinidad. Referring to Sir Frederick's optimistic remarks regarding the prospect of eradicating bovine tuberculosis in this country by means of periodical tuberculin-testing and clinical examination of cattle by the new State Veterinary Service, he asked if Sir Frederick believed that such eradication was really probable within a reasonable period under the conditions prevailing in this country, which differed so greatly from those in the United States and Canada, where the success of the eradication campaign was well known.

Dr. J. D. ROLLESTON said that a closer collaboration between the medical and veterinary professions had been facilitated by the creation in 1923 of the Section of Comparative Medicine, of which Sir Thomas Clifford Allbutt had been the first president, and Sir D'Arcy Power the third, and also by international congresses of the history of medicine in which several veterinarians of different countries had taken an active part.

The earliest examples of the coexistence of epidemics and epizootics, were to be found in Homer and Thucydides, who described pestilences among human beings, accompanied by similar diseases with a high mortality among horses, cattle, dogs, and birds. In more modern times a similar coexistence of epidemics and epizootics had been reported in the case of influenza, plague, dengue, cholera and scarlet fever in the seventeenth, eighteenth and nineteenth centuries (Hirsch, 1883; Creighton, 1891, 1894).

REFERENCES.

- CREIGHTON, C., "History of Epidemics in Britain", 1891, 1, 558, 608; 1894, 2, 354, 361, 371, 372, 398, 719.
HIRSCH, A., "Handbook of Geographical and Historical Pathology", 1883, 1, 38, 40, 78, 477, 479.
HOMER, "Iliad", 1, 48, *et seq.*
THUCYDIDES, 2, 47-54.

Dr. G. CLARK TROTTER said that, with regard to increased veterinary inspection, he wished to draw attention to the lax state of affairs which allowed leakage of meat of condemned carcasses from knackers' yards, ostensibly sold for dog food, &c., to be sold for human consumption. Such action was very difficult to trace and prove. It would be an advantage if knacker meat could be artificially coloured in some way to distinguish it, and thus prevent its being passed off for human consumption, pending more efficient and compulsory inspection.

Colonel C. A. GILL said that foot-and-mouth disease was of particular interest from the epidemiological point of view, and wondered whether he was correct in assuming that the theory that this disease was imported into England by migrant birds had been abandoned. If the disease was now regarded as permanently endemic in this country, it would be interesting to know the reservoir of infection, and whether healthy cattle were the carriers, or whether the disease was spread by sick animals, or by animals that had recovered from the disease.

According to newspaper reports, the disease often appeared in remote farms in circumstances which appeared to preclude the possibility of contact with known centres of infection, and this led him to ask whether the destruction of animals in infected areas, which was very costly, gave promise of eventually eradicating the disease.

Sir FREDERICK HOBDAY (in reply to Sir Weldon Dalrymple-Champneys) said that the European bat had not in any way been suspected of being implicated—as had the vampire bat of Trinidad—in the transmission of rabies. With regard to the prospect of eradication of

tuberculous cattle: under present conditions in Great Britain, he certainly believed that the establishment of a well-organized Veterinary State Service would go a long way towards the attainment of this object.

In reply to Colonel Gill: The spread of foot-and-mouth disease by the migrating birds had not been definitely proved to be serious; the actual source of the periodical outbreaks occurring from time to time could not always be traced satisfactorily. There was no doubt, however, that the stamping-out method, in countries where it could be carried out was, economically and on all other grounds, the best method to adopt.

Great Britain had the great advantage of being an island, and, in this respect, had many advantages over continental countries with land frontiers, to which it was so difficult to apply quarantine or similar efficient measures for disinfection.

Section of Medicine

President—Sir CHARLTON BRISCOE, Bart., M.D.

[October 27, 1936]

DISCUSSION ON THE TREATMENT OF PLEURAL EFFUSIONS

Opening Paper

By G. MAURER, M.D.

(*Medical Superintendent, Schatzalp Sanatorium, Davos*)

INSTEAD of giving a comprehensive survey of the field, I intend to deal with some of the more interesting aspects of the problem, but I hope that other points will be brought forward during the discussion.

When a pleural effusion is diagnosed, the clinical picture, in conjunction with exploratory puncture, gives us the best clue to the character of the pleurisy. In septic conditions we may see staphylo-, strepto-, pneumococci, &c., grow on the culture media. In one case I even found a pseudo-diphtheritic bacillus. The differentiation between transudate and tuberculous effusion is not difficult. The specific gravity of a transudate does not exceed 1015, while that of tuberculous effusion is always over 1018; the albumin content of the former seldom reaches 3%, whilst in the latter we find 4% or more and, finally, the fibrin content of the transudate is remarkably low. The transudate, therefore, in marked contrast to exudate, does not coagulate at all, or only very slowly. These analyses, in conjunction with the clinical findings, will enable us to distinguish between transudate and tuberculous exudate.

We must not rely too much on bacteriological examination and animal inoculation, as the results are negative in many cases which are undoubtedly of tuberculous origin. I have found bacilli more frequently after a basal, than after a higher exploratory puncture; gravity appears to play a part here.

It would be going too far to say that rheumatic pleurisy does not occur, but it is so uncommon that this diagnosis should only be made when another definite rheumatic lesion is present in the body.

Polyserositis tuberculosa is sometimes confused with cardiac decompensation. Analysis of the pleural fluid, as described above, should clear up the diagnosis. The differential diagnosis between pleural tuberculosis and new growths is not always easy. If glandular metastases are missing and we find no cancer cells in the fluid, the diagnosis can always be cleared up by a thoracoscopy.

Syphilis of the pleura is so rare and, when present, is accompanied by so many unmistakable signs of syphilis elsewhere in the body, that the diagnosis is clear.

What are the lines of treatment once we have established that our patient is suffering from a tuberculous pleural effusion? We should avoid any considerable removal of fluid during the febrile exudative phase. A highly inflamed serosa, irritated by aspiration, may change a serous into a purulent exudate.

When the pleural exudation ceases and the resorption phase sets in, we have to do an air replacement, as Burrell, Chandler, and others recommend. Naturally I am not talking about the pleurisy which only lasts a few days, where we have difficulty in obtaining even a few drops of fluid for examination. The initial pleurisy is not a disease but a symptom of tuberculosis. It is due to dissemination from a focus, almost invariably to be found in the lungs, usually in the homolateral side, and varying from a small caseous gland to an excavating process. I believe that propagation by the

lymphatic route is more frequent than by the blood-stream or by spread in continuity from a superficial lung lesion. Once the pleural effusion has developed, when we see the patient for the first time, we cannot form an opinion about the condition of the underlying lung. We know it is extremely probable that there is an active lesion in the lung, but we know nothing about its extent or character.

Tapping without air replacement is risky because (1) the patient may collapse or even die because of the sudden alteration in intrathoracic pressure, (2) the abrupt expansion of the lung will irritate its lesions, (3) it may mechanically mobilize a tuberculous thrombus in the lung or in the serosa—thus we sometimes see meningitis after fluid aspiration without air replacement, (4) if a superficial, i.e. subpleural, focus, has been the cause of the effusion, we risk a purulent exudate or even a spontaneous pneumothorax.

Air replacement avoids all these risks and is performed because it hastens resorption. One may dispute the necessity of fluid removal at all, but I cannot recommend it too strongly in every case of large initial pleural effusion. In my sanatorium, every fifth patient suffering from pulmonary tuberculosis gives a history of pleural effusion months or years before cavities developed in the lungs. In these cases complete pleural obliteration renders a pneumothorax impossible and one feels sorry, because an air replacement of the pleural effusion, continued for some time as an artificial pneumothorax, would have prevented the development of severe tuberculosis. The hydro-pneumothorax, which exists after the air replacement, has to be kept up until the exudate has completely disappeared. The lung is then partially re-expanded, leaving just enough gas in the pleural cavity to prevent adherence of the pleural layers and to allow sufficient space for refills. The time has now come when X-rays, sputum tests, and all the other diagnostic methods, will show us whether it is advisable to continue the observation pneumothorax as a therapeutic pneumothorax.

I believe that, in this way, small but active lesions are often quickly and easily healed. Without collapse therapy these foci may also heal, but in 40% of cases, according to Burrell's statistics, they develop into clinical pulmonary tuberculosis. When we have symptoms of appendicitis we remove the appendix, although only 10 to 15% perforate without operation. In my opinion, therefore, it is better to continue an observation pneumothorax unnecessarily for some weeks or months in a certain number of patients, than to be confronted later on with the difficult problem of treating extensive, and often bilateralized, disease in the presence of a totally adherent pleura. As a final inference, I consider that in every case of dry pleurisy, even the most transient, a skiagram should be taken and the sputum tested immediately, because once the inflammation of the serosa has passed off, it will be too late to decide whether an artificial pneumothorax is indicated or not.

In the small percentage of cases in which the clear yellowish fluid becomes purulent the prognosis is bad. The body must have very low powers of resistance indeed when the pleural reaction to tuberculous infection is a purulent secretion. Repeated and complete aspirations of pus may help to diminish the size of the empyema cavity by pleural retraction and symphysis. As a rule we have to perform thoracoplasty later on; it is always better to defer this intervention until the acute exudation is over and fever has subsided.

The more superficial the lung focus, the greater the risk of a spontaneous pneumothorax, owing to destruction and perforation of the visceral pleura. The end-result of this is generally a mixed infected empyema. This complication requires a thoracocentesis and daily pleural lavage, at first with normal saline, later on with antiseptics. In these serious cases one should not perform thoracoplasty until the acute symptoms have disappeared. Our results are so poor that I would like to hear if English chest surgery, which has made such remarkable progress lately in many directions, has found a more successful method of treatment.

The ordinary clear artificial pneumothorax effusion is, for me, always a problem. On the one hand, the pressure of the exudate may reduce the volume of the lung to

a minimum. In the course of time inflammation thickens the visceral pleura and the final stage is a residual pneumothorax, with a lung which it is impossible to expand because it is encapsuled in a thickened and inelastic pleura. On the other hand, a progressive pleural symphysis often begins during the course of an effusion and leads to total obliteration of the pneumothorax.

I believe that both complications can usually be avoided. We do not interfere with the fluid during the acute exudative phase. At this stage, if we have to diminish the pressure in order to relieve cardiac embarrassment or other symptoms of mediastinal displacement, it is better to withdraw air. When the temperature has dropped to normal and the exudate has ceased to increase in size, I aspirate all large pneumothorax exudates, leaving the end-pressure distinctly negative. By taking off, sometimes fluid, sometimes gas, I obtain a partial re-expansion of the lung. How far one can go with this partial re-development of the lung depends upon the size and situation of the pulmonary lesions. Because of the continuously negative intrapleural pressure the pneumothorax lung moves with the respiratory excursions under the fluid. This massage prevents the visceral pleura from becoming too thick or losing entirely its elasticity. When the exudate has been absorbed one usually sees the base of the lung adherent to the diaphragm and the lower thorax wall. At this stage, the extension upwards of the symphysis between lung and chest wall is checked by more frequent and larger refills. If it, nevertheless, shows a tendency to increase to an undesirable degree, we can carry out temporary oleothorax. In this way we avoid a residual pneumothorax, because the visceral pleura retains some of its elasticity and the pneumothorax cavity is smaller.

A pneumothorax lung containing large cavities or basal foci must be kept collapsed even during the effusion, and here, of course, partial redevelopment of the lung is contra-indicated. The intrapleural pressure must always be adapted to the extent and situation of the lesions, but I incline to sacrifice to some extent the ideal collapse of the lung during the effusion period, in the interests of a subsequent easy re-expansion. The residual pneumothorax, which we see in practice only too often, is nearly always the result of maintaining an extreme collapse of the lung during the treatment of an effusion. In not too pronounced cases, a diaphragmatic paralysis may be sufficient to bring the visceral and parietal pleura into contact. In more extreme cases we have to close the residual pneumothorax by a thoracoplasty. This residual pneumothorax should not be left permanently; the risk of a later perforation into the lung is too great.

As regards progressive pleural symphysis: When the lung base, in spite of repeated refills, even with slightly positive pressure, begins to adhere to the diaphragm and chest wall, a pleuritis fibrosa or sero-fibrinosa is invariably present, as I have found, with the thoracoscope. The fibrin coagulum forms bridges between the visceral and parietal pleural layers. By organization and retraction of these fibrin masses, the lung is irresistibly drawn out and fused to the chest wall. The progressive symphysis is, therefore, always preceded by fibrin formation. Here the oleothorax saves the remaining pleural cavity. I allow the oil to remain in the pleural cavity from four to, at the most, six months. By this time the pleuritis fibrinosa ought to have settled down. The oil, a foreign body, is then replaced by air. In my opinion the progressive symphysis is the only—and important—indication for oleothorax.

The few artificial pneumothorax exudates which become purulent should, of course, be completely removed. I have not seen very favourable results from oleothorax treatment in these cases.

In dealing with the mixed infected empyemata, lavage with pantosept, which is somewhat similar to Carrel-Dakin fluid, can be tried, but if improvement is not noted within a few weeks, thoracoplasty should not be delayed, in view of the danger of amyloid disease.

Having discussed at some length the dangers of pneumothorax effusion, I must

add that now and then the exudate has a beneficial effect. We know from experience that in cases of mobile mediastinum the results of pneumothorax treatment are poor. This is because it is impossible to collapse the lung properly. We are glad to see an effusion occur in these cases. The resulting pleural thickening fixes the mediastinum. Unfortunately it is just here, where exudate would be beneficial, that it seldom forms. So I remedy the situation by producing an artificial exudate. The fixity of the mediastinum is so important from a therapeutic point of view, in pneumothorax treatment, that attempts to immobilize the flaccid mediastinum artificially have not been wanting. I employ 50% glucose solution. This hypertonic solution, when injected into the pleural cavity, produces bursting and desquamation of the endothelial cells, inflammation of the subserosa, and a pneumothorax exudate. When serous surfaces, denuded of their endothelium, are allowed to remain in contact for a sufficient length of time, the opposing surfaces adhere. In this way hernial pouches are obliterated and the mediastinum, as a whole stiffened, slightly by thickening of its pleura, but mainly by adhesions to the medial aspect of the lung. As this surface of the lung becomes at the same time adherent to the anterior and posterior borders of the mediastinal partition, i.e. to the spine and sternum, the partition as a whole becomes much less yielding.

From statistics we know that the cure rate of bilateral pneumothorax treatment is remarkably low, namely 12%, the reason being that it is impossible to collapse either lung effectively when a pneumothorax is present on both sides. If we fix the healthy part of the lung to the chest wall we can produce better collapse and rest of the diseased part. It is astonishing to see how much more effective the double pneumothorax is rendered in practice by the application of this new principle.

Dr. Burton Wood: The commonest cause, to-day, of pleural effusion in the tuberculous is trauma. Better than treating an effusion is not to provoke one; to remember that a blunt needle will lacerate the pleura, that a drop of spirit left in a needle may cause intense irritation, that cold air injected into a warm pleural cavity may provoke a reaction or a positive pressure lead to effusion by the stretching or tearing of adhesions. The man who cannot use his needle as an artist should turn to less delicate work. Any pleural puncture may be the first step towards a thoracoplasty.

Many pleural effusions require no active treatment. They are benign and may be protective in their effect, if not in their intention. Thus, a pleural effusion is the commonest manifestation of intrathoracic tuberculosis in childhood. It appears to be analogous to other reactions of allergic type seen in child contacts. Such effusions have little effect on health, sometimes disappear very rapidly, and are very rarely followed by parenchymatous disease.

Some of the adolescent pleuritis, like erythema, are of similar type. For this reason I feel that a young person with a "simple" pleural effusion and who is possibly in a hypersensitive state, should not be exposed to the risk of further infection, e.g. by sharing a sanatorium cubicle with an "open" case of pulmonary tuberculosis.

What is the after-history of patients whose lungs were apparently otherwise sound at the time of an effusion? We have always been taught that the expectation of subsequent phthisis is about 40% to 50%, but recent figures from Scandinavia suggest that 90% of the patients make a lasting recovery. Time has not allowed me to make an exhaustive inquiry, and I must not claim statistical accuracy, but in a series of thirty cases comprising young persons of the working class (15 to 35 years of age, at onset), observed during an average period of nearly five years, 27 patients have remained well, and the three who have died were all examples of bilateral pleurisy. Two of these died of generalized tuberculosis, and the third is stated to have caught a chill while travelling to a sanatorium and to have died not long after admission.

Before the advent of chest radiology the condition of the lung underlying an

effusion must have been often in doubt, and many of the patients diagnosed as having pleural effusions would to-day have been diagnosed as having pleuro-pulmonary tuberculosis. The factory girl, convalescent from pleurisy with effusion, need no longer despair if her purse does not permit her to follow the advice of a well-known textbook—to enjoy a generous dietary, to take prolonged holidays, and to spend the first winter at a high Alpine station.

If effusion is suspected, X-ray examination should precede exploration. Blind tapping is only justifiable for the relief of urgent symptoms, and haphazard aspirations in the bedroom are to be deprecated. If the disease runs a favourable course, the fluid will absorb spontaneously, but if it is of less benign type, aspiration will only be followed by a fresh outpouring of fluid, which will thicken as aspirations are repeated. The end-result will be a chest still containing fluid—but empyematous fluid. It is true that fluid, if left, will ultimately cause pleural thickening, but an obliterative pleurisy, with the fibrosis to which it gives rise, is a conservative process. Fibrosis begins where tuberculosis ends. I have sometimes used oleothorax to check a too hasty obliteration.

The presence of a tuberculous focus in the underlying lung is sometimes assumed, and this has given rise to the practice of air replacement and the maintenance of a pneumothorax for a period of some months to protect the lung. This is treatment based on speculation, unless the effusion is known to cover diseased lung.

When the large size of an effusion causes mediastinal displacement or distress, air or oxygen replacement is, of course, necessary, but it is useless to try to prevent re-accumulation by pneumothorax. If hectic fever persists, an aspiration will sometimes be followed by a fall of temperature. It is justifiable to try the effect of this, with or without replacement, but repeated aspirations are undesirable.

Many of the effusions complicating artificial pneumothorax are benign in their effect. An incomplete collapse is sometimes converted into a complete collapse and a cavity held out by adhesions, closed (before their sections can be considered) by the beneficial effect of an effusion. If an effusion rapidly fills the pleural space, it is tempting to replace it by air in the hope of maintaining a controlled collapse. Replacement is, however, usually rapidly followed by re-accumulation, and recurrent aspirations bring the risk of empyema. Unless an unclosed cavity persists it is, in my opinion, better not to interfere. A natural serothorax sometimes forms a good substitute for a pneumothorax, and the effusion absorbs slowly.

As intrapleural pneumolysis brings some added risk of pleural effusion, I question the wisdom of the increasing practice of dividing adhesions in the early weeks of a pneumothorax before its efficacy can be fairly judged, and when neither expectoration nor radiography indicate that a cavity formerly recognized is still patent.

When a serous effusion is followed by a tuberculous empyema, anxiety is inevitable, though a tuberculous pleural abscess may remain latent for years, may not appear to affect the patient's health, and may ultimately become completely encapsuled. But the sword of Damocles hangs above the patient's head, and the threat of ultimate perforation of the lung with bronchopleural fistula and secondary infection remains.

Professor Rist has pointed out, for our comfort, that though in cases of chronic tuberculous effusion the fluid may swarm with tubercle bacilli, the reaction of guinea-pigs to inoculation is sluggish or negative. He claims that the fluid of these tubercle-rich effusions exercises an inhibitory influence on the growth of the bacilli. Gloyne agrees that a tuberculous exudate contains immune bodies. Repeated aspirations of tuberculous empyemata involve the gravest of all risks—that of secondary infection. The risks of thoracoplasty in these cases are, I think, graver than those of a symptomless tuberculous empyema, and I suggest that conservative treatment is still the best that can be offered in most cases, especially in the young.

In the treatment of an infected tuberculous effusion the need for action is urgent, but in the less virulent cases, before instituting closed drainage by intercostal catheter and negative suction, I feel that an attempt to avoid drainage is justifiable, provided

that it is not persisted in too long. Gomenolized oil does not mix well with pleural fluid, and a gelatine flavine solution, as recommended by Crockett, is preferable. This mixes intimately with the pus and does not, like oil, float on the top. Here is an example of its use :—

A child, aged 13 years, undergoing artificial-pneumothorax treatment for acute tuberculous disease of the right lower lobe, developed first a serous effusion and then a fœtid empyema. A gelatino-thorax was induced and within a week the pus was almost odourless. Later, closed suction drainage and pleural lavage with flavine gelatine and Dakin's solution were employed, and at the present time the patient's general condition is good, the pleural cavity is obliterated, and although two sinuses persist in the chest wall, a small plastic operation should suffice to close them.

For the chronic, secondarily, infected tuberculous empyema we are left with a permanent tube or a plastic operation as alternatives. There can be no fixed rules to guide us in this choice of evils. The drastic type of thoracoplasty which is necessary to close a thick-walled pleural space can only be justified if the patient has a fair chance of recovery. The younger the patient, the less is the chance, not only of survival of operative risk, but of his escaping contralateral disease. Tuberculosis is not merely a local disease, and to act as if it were may only result in added torture to the dying. If, however, the disease has become stabilized, and the patient's general condition is fairly good, a determined effort to close the pleural space is justifiable. Here, for example [skiagram shown], is an illustration of the chest of a poor boy who after prolonged but ineffective sanatorium treatment was sent to an infirmary, there to await his end. He had heard of thoracoplasty and, still undaunted, insisted on being transferred to Victoria Park Hospital for surgical treatment. There he has been under the care of my colleague, Dr. H. V. Morlock, and with the help of the surgeons, a secondarily infected tuberculous empyema in a capacious pleural cavity has been reduced already to a mere slit in the chest wall.

Dr. S. Vere Pearson said that fuller experience seemed to him to make it more difficult to lay down hard and fast rules. In the treatment of pleural effusions every case had to be taken on its merits. There was still much to learn. For example, had anyone yet discovered whether one type of needle was more conducive to effusions than another in the conduct of an artificial pneumothorax? Prolonged continuity of treatment was necessary for tuberculous patients, but it was not always easy to secure. Someone who knew the case for as long as possible should be primarily responsible. He was glad that Dr. Maurer advised that oil of gomenol should not be left in the chest for longer than six months. He felt sure this was the proper practice. In connexion with the consequences of a bronchial fistula—almost always dire—he believed that the condition of the pleura was of secondary importance to that of the underlying lung. Regarding encysted collections of fluid, some of these were best left alone.

Dr. L. S. T. Burrell agreed that there was a danger of thickened pleura, with fibrosis of the underlying lung, occurring if the effusion were left too long; this was more likely to occur as a result rather of an old-standing effusion than of a large one. It was the length of time, not the quantity of fluid, that mattered.

He did not recommend gas replacement as a routine in tuberculous pleural effusion because he found that this often prevented the lung completely re-expanding for a long time; he had known cases go on for several years. In ordinary pneumothorax treatment the lung re-expanded soon after refills had stopped, but when complicated by effusion this was not so.

In most cases of simple pleural effusion the exudate had become absorbed at the end of a few weeks, and the patient was apparently well. This was the time at which careful supervision and sanatorium routine were required, so that any evidence of infiltration of lung tissue could be detected and treated at once.

Another objection to gas replacement was that a lesion sometimes began in the opposite lung, and when this happened it might necessitate a pneumothorax on that side, instead of on the side with the old effusion.

Section of Neurology

President—C. M. HINDS HOWELL, M.D.

CASES SHOWN AT THE NATIONAL HOSPITAL, QUEEN SQUARE, W.C.1,
FEBRUARY 18, 1937.

Paget's Disease of the Skull associated with a Pituitary Neoplasm. —MACDONALD CRITCHLEY, M.D.

Mrs. X, aged 62, has had frequent headaches for the last forty-two years—i.e. since her first confinement—each attack being associated with nausea, but there was no vomiting or teichopsia. During the last two years the headaches have become more intense, and different in character. Two years and a half ago vision began to deteriorate—at first in the right half of the right field of vision. Some indefinite visual defect in the left eye was noticed four months ago. The patient thinks her head has always been large, but is sure there has been no increase in size during the last ten years.

Previous health.—The patient was born with a crippled right leg. At the age of 41 she had a transitory left-sided stroke, with disordered speech. Six weeks later, "something went bang in her head"; ever since, she has been conscious of a continuous noise in the right ear and temple.

On examination.—Cranium: Uniformly enlarged; circumference 61 cm. No obvious skeletal change elsewhere. A systolic bruit is audible in both temples and can be inhibited by compression of the corresponding carotid artery.

Vision: Right $\frac{6}{24}$; left $\frac{6}{6}$. Fields: Complete temporal defect on the right side and an upper temporal defect on the left. Fundi: Optic atrophy on right side.

Central nervous system: Mild right-sided hemiparesis with dysplasia.

Radiogram of skull: Shows the changes of advanced Paget's disease. Optic foramina normal. Erosion of sella turcica.

The question here is whether we are dealing with an accidental association of pituitary tumour with Paget's disease of the skull. In answer to a question by Dr. Garland, I said I felt that the changes seen radiologically were typical of the latter disease. In my opinion, the tinnitus and the bruit were extra-cranial, rather than intra-cranial, in origin, and for that reason I did not believe that the erosion of the sella turcica was due to aneurysm. The character of the field changes, and the fact that the optic foramina appear normal in size and shape in the radiograms of the skull, argue strongly that the visual defect is the result of the pituitary tumour rather than of the Paget's disease.

Amentia, Familial Cerebellar Diplegia, and Retinitis Pigmentosa.— R. M. STEWART, M.D.

H. C., female, aged 28.

History.—One of seven siblings. An elder sister who died in January 1937 showed similar clinical features. No history of nervous disease or retinitis pigmentosa in antecedents.

History of protracted labour. Condition first noticed by mother six months after birth; patient took no interest in surroundings and made no effort to sit up. Institutional treatment from the age of 3 years.

On examination.—General condition good. Marked dorsal kyphosis with slight scoliosis, convexity to right. Circumference of head 22 in.; C.I. 72.

Mental state: Placid; low-grade imbecile. Mental age by Burt's scale 2.5 years. Habits fairly clean. Speech limited to a few words. Articulation slurred, jerky, and explosive.

Cranial nerves: Visual acuity reduced. Fundi: Retinitis pigmentosa; bone corpuscle spots of pigmentation; small retinal vessels. Pupils and ocular movements normal. No nystagmus. Slight double ptosis. Facial movements weak and absence of lines of expression; fixed smile.

Motor system: Limb movements free, but weak and inco-ordinate. Dysmetria in upper limbs. Can stand when supported; makes wildly ataxic movements with lower limbs when trying to walk. Marked muscular hypotonia. Muscles soft and flaccid; abnormal laxity at all limb joints. Coarse tremor on voluntary movement. Sensations: ? normal.

Reflexes: Abdominals not obtained; plantars, flexor response; tendon reflexes present and equal.

Cerebrospinal fluid normal. Blood Wassermann reaction negative.

Discussion.—MR. ARNOLD SORSBY said that when the Tay-Sachs disease became recognized as a clinical entity there was a tendency to regard every cerebral degeneration associated with retinal changes as a form of that disease. So much did this tendency persist that when the totally distinct clinical entity of Batten-Mayou disease was clearly established, people regarded it as a modification of the Tay-Sachs disease. It was thus that the erroneous titles of "infantile amaurotic idiocy" applied to Tay-Sachs disease, and of "juvenile amaurotic idiocy", applied to Batten-Mayou disease, had become firmly established. Apart from these two groups, there was also a third variety of cerebro-retinal dystrophy; the Laurence-Biedl syndrome. It would therefore be wise, now that evidence was coming forward of the existence of a group of cerebello-retinal degeneration, not to regard every reported case as an example of one and the same disturbance. His own impression, from the reading of the various cases that had been reported since 1901, and from a study of the family under his care, was that there were probably as many different forms of cerebello-retinal degeneration as there were of the cerebro-retinal type. At any rate dogmatism should be avoided at this stage.

Dr. D. E. DENNY-BROWN asked whether there was any evidence in this patient, or in the history of other members of the family, that this was a progressive lesion, and whether the retinal condition had progressed to complete blindness. In the examples that he had seen of that type of disturbance, where retinitis pigmentosa occurred with spastic paraplegia, both the conditions were progressive, and had begun at the ages of from 18 to 25 years. That type, of course, appeared to be more in line with the conception of late "cerebro-macular" disease.

Dr. R. M. STEWART (in reply) said that in both the cases referred to there had been definite progression of the symptoms, the two sisters having become more helpless as they grew older. As the retinitis pigmentosa had only been detected last year he could not say how far it had progressed, if at all. But the fact that the sister who had died recently, and who was six years older than this patient, had had all the physical signs, including those in the retina, in a more marked degree than in the younger sister, suggested a steady progression.

Colloid Cyst of Third Ventricle.—GEOFFREY JEFFERSON, F.R.C.S. (Referred by MACDONALD CRITCHLEY, M.D.).

M. R., female, aged 45.

History.—For seven years patient has had intermittent attacks of headache and vomiting, with occasional major generalized convulsive seizures. Transient papilloedema observed after the first attack. Psychotic symptoms with delusions of persecution at intervals during this period. Stuporose during last week.

On examination.—No positive neurological signs except bilateral chronic papilloedema. Ventriculography showed symmetrical dilatation of the lateral ventricle, but no air in the third ventricle except a thin crescent in its anterior end.

Operation (May 28, 1936).—Excision of circle of right frontal cortex; third ventricle explored through foramen of Monro; colloid cyst of third ventricle found and removed.

There was this long history of intermittent headache and occasional attacks of vomiting, with recovery afterwards. There were no neurological signs; the only sign was papilloedema. The diagnosis rested largely on the ventriculograms. As far as the ventricle was concerned, it was evident that there was internal hydrocephalus, but in the view taken with the head fully extended over the end of the table, so as to get the air to go up into the third ventricle, that ventricle had not filled, but one could see that the foramen of Monro was reduced in size. There was a slit of air in the anterior end of the third ventricle, but nothing behind that. That same picture was given in three separate films. There was a chance that these non-fillings might be due to air-locks, but the foramen of Monro was very narrow. At the Manchester Royal Infirmary Dr. Twining worked out with me the radiography of the third ventricle, and the filling defects in the different lesions.

Therefore I operated immediately, turning down a right frontal flap and excising a circular piece of the right frontal cortex. When the ventricle was opened, the foramen of Monro was identified by the veins leading to it and by the choroid plexus coming out. It was blocked by an opaque grey cyst. The cyst was picked up and punctured; it was very difficult to aspirate. To try to puncture one of these cysts in an emergency would be of little use. When I had emptied the cyst and extended the foramen forward by incising the anterior pillar of the fornix, it was easy to deliver the cyst and remove it.

The patient made an uninterrupted recovery, and is now, apparently, in good health. At no time did she have difficulty in turning her eyes to the opposite side. Of seven patients dealt with by this method of approach, only one had difficulty in turning the eyes, and that difficulty lasted only seven days.

Discussion.—Dr. MACDONALD CRITCHLEY said that he had seen this patient about eighteen months ago at another hospital, whence she was transferred to Queen Square. In hospital there were practically no abnormal physical signs except papilloedema, but, in consideration of the history, it was thought that a third ventricle tumour was the most likely diagnosis. She had previously been an in-patient in one or two mental hospitals. It was interesting that at one of them, some years ago, the diagnosis of third ventricle tumour had been made; even at that time she had papilloedema. On the strength of the suggestive history a ventriculography was carried out and had appeared to show a surprisingly normal third ventricle. Mr. Jefferson, whom he had asked to see the patient, had, by a stroke of genius, suggested another ventriculography; the result showed, as Mr. Jefferson now demonstrated, a definite third ventricle tumour.

Though this patient had made a post-operative recovery, she had recently reported to hospital with a return of her depression and with ideas of persecution. The possibility of a recurrent depressive psychosis independent of the third ventricle tumour was very great.

Mr. JEFFERSON said he had forgotten to mention that at the operation it was found that the upper part of the cyst was covered with a film of brain tissue. The only knowledge he had at the time was Dandy's remark that the tumour arose from the ependyma or the choroid plexus. It was consistent with a paraphysial origin that this layer of glial tissue was present, the tumour descending though the roof of the third ventricle.

Two Cases of Left Frontal Lobectomy.—GEOFFREY JEFFERSON, F.R.C.S.

I.—(Referred by Dr. C. P. SYMONDS.)

N. W., female, aged 32.

History.—Blindness in left eye for fifteen years. Three years ago onset of *petit mal* attacks and slight failure of memory. Complete anosmia for three months.

On examination.—Complete bilateral anosmia. Left eye blind, with advanced primary optic atrophy. Right eye had papilloedema of 4 diopters but normal vision.

Operation (April 30, 1936).—Left frontal parasagittal meningioma and olfactory-groove meningioma removed after partial resection of left frontal lobe.

II.—(Referred by Dr. J. PURDON MARTIN.)

T. L., male, aged 42.

History.—Five years ago onset of *petit mal* attacks. One attack of loss of consciousness three years ago. Left frontal headache and slight impairment of memory for two years. Slight blurring of vision during last nine months.

On examination.—The only positive signs were slight weakness of the right lower face and diminution of the right abdominal reflexes.

X-ray examination.—Large irregular calcified area deep in left frontal lobe.

Operation (December 23, 1936).—Removal of large deep frontal cyst after resection of part of left frontal lobe.

I am showing these two patients together, not from the point of view of pathology, but as examples of removal of the left frontal lobe.

In the first case two tumours were present, the first was small, and did not account for the blindness. When it was out and I had another look round I found the second and larger olfactory groove meningioma. The patient had had bilateral anosmia. The left frontal lobe was resected back to immediately in front of the middle fossa. The sphenoid wing is less than a centimetre behind the level of section, and it was carried straight up to the falx and the frontal lobe removed. What effect did removal of the left frontal lobe have? The operation was done under gas-and-oxygen, and lasted five and a half hours. Half an hour after being put back to bed she was waking up, and I asked her how she was; she replied "All right, but very frightened". Asked what about, she replied that it was about the operation she was to have. When told that she had had it, she refused for a time to believe the fact. She is able to do all she has to do and wants to do; she keeps house, and does her own washing. She also has a good memory, she tells us. She has to wear glasses, but she reads easily, and remembers what she has read.

In the second case, in which the operation took place only six weeks ago, the patient tells us that he can do everything as well as he could before the operation, and he does not think his memory is any worse. He does not read much, but then he never did. We took out the frontal lobe; the next slide shows the amount of frontal area removed.

I have now removed seven frontal lobes successfully; four right-sided, three left-sided. The removal seems to make remarkably little difference to the patients. If there is much psychotic change it means that the tumour has spread across the mid-line and that both lobes are involved. I do not know whether, in that case, it would be safe to try to carry out removal; one might not know, until the operation was in progress, whether the other side was involved. Long-standing frontal gliomata are apt to extend from one side to the other.

The results of these removals are sufficiently encouraging to warrant going on.

Discussion.—Dr. J. PURDON MARTIN said that in the second case, that of his own patient, he was particularly interested in the skiagram. As Mr. Jefferson had said, if there had not been several tumours, the condition would have been passed for aneurysm. Next he thought the lesion might be tuberculoma, but decided that the line forming the ring was much too smooth for tuberculoma. He believed Dr. Greenfield had concluded that it was probably a congenital tumour of the nature of an epidermoid.

What disturbances of function could be detected in these patients from whom a large part of one frontal lobe had been removed? The most apparent changes were on the emotional side. The most striking was a lack of reserve. This was noticeable in both of these cases, and he had observed it in other cases of frontal lobe lesions. Another peculiarity was that the patients were constantly somewhat elated; they were jolly and inclined to be facetious. On the intellectual side the changes might be summarized as a lack of "depth"; this included a failure to see the various aspects of a situation, or implications of what was said.

He agreed with Mr. Jefferson that mental impairment was not pronounced unless both frontal lobes were affected, or unless the fibres connecting the two frontal lobes were involved. In the case of frontal tumour the onset of obvious mental symptoms usually indicated the spread of the tumour to the corpus callosum.

Mr. JEFFERSON, in reply to a question, said that no technique was needed to keep the remaining parts of the brain in position; they looked after themselves extraordinarily well. In both these cases the removal had been carried out in order to obtain access to the tumours, which were so far back that removal would have been impossible otherwise.

He agreed with Dr. Martin that this operation could not be performed on all patients irrespective of their intellectual background. These particular patients were not a very good index, they were average working-class folk. Another patient, whom he had shown at a meeting of the Association of Physicians in Manchester, had exhibited that same lack of reserve which had been mentioned, but which he (Mr. Jefferson) had attributed to the physicians rather than to the patient. None of the patients in the cases of left-sided removal had shown any sign of aphasia.

Occipital Lobectomy.—E. A. CARMICHAEL, M.B.

L. P., a boy, aged 14.

History.—Full-time child; labour difficult. Normal development. In September 1934 began to have two types of attacks: (1) In which he experienced coloured lights in the left upper quadrant; (2) in which he would drop objects out of his hand. In several of these he lost consciousness. The attacks became more frequent.

On examination (February 1936).—A bright and intelligent boy, who co-operated well. The following abnormalities were found: (1) A defect in the left lower quadrant of the field of vision; this was more especially evident after an attack; (2) a defect in the skull in the right occipital region (confirmed by X-rays). The cerebrospinal fluid was normal. A bilateral ventricular tap was carried out and air was injected. The right ventricular fluid was slightly yellow and contained 55 mgm. of protein; the left ventricular fluid was normal. X-rays showed a distension of the right posterior horn reaching out to the defect in the bone.

Operation.—Right occipital lobectomy performed by Mr. Geoffrey Jefferson in May 1936. Following this, the boy had, for a few days, considerable sensory disturbance down the left side, but this eventually cleared up. Three days after operation, confrontation tests showed a complete left-sided hemianopia with sparing of the macula. In the succeeding weeks this was frequently confirmed by perimetry. In October 1936, the patient had an acute headache, stiff neck and a rise in temperature. The lumbar fluid was turbid, containing a large number of polymorphonuclear cells, but no organisms. Following this acute illness, the fields of vision showed, by confrontation tests and perimetry, a left homonymous hemianopia splitting the macula. Marked sensory disturbance was demonstrated down the left side. General improvement has taken place and when the boy was seen, in January 1937, the field of vision showed left homonymous hemianopia splitting the macula.

Discussion.—Dr. MACDONALD CRITCHLEY said that this was a most important case, as it shed considerable light on the vexed problem of the cerebral representation of the macula. For some time past he had inclined to the view that the macula was probably represented bilaterally, and the present case appeared to bear out that idea. In Foerster's opinion the macula was probably represented bilaterally, by way of a double decussation: first a partial decussation in the optic chiasma, then a second decussation—complete, or almost complete—in the corpus callosum, or possibly in the posterior commissure. Foerster had described an excellent clinical case in point:

The patient had a lesion of one occipital pole of such magnitude as to involve the whole of the visual cortex, and like the present patient, had hemianopia, with a sparing of the macula. Operation subsequently became necessary, in the course of which the surgeon incised the splenium of the corpus callosum. Thereafter there was a complete homonymous hemianopia passing cleanly through the fixation-point.

Dr. R. M. STEWART asked a question as to the nature of the cyst.

Mr. JEFFERSON (in reply) said that the cyst had been traumatic, and the patient had lost bone spontaneously under the area without an open wound. Occasionally the same thing happened in the case of the carpal bones, owing to the severe stress. It seemed to be almost always the case that when bone disappeared a ventricular blow-out occurred; there had been such an injury to the underlying brain that it necrosed, and there was a cavity *ex vacuo* communicating with the ventricle and causing the fits. Therefore this boy's occipital lobe had been taken away in order to cure the fits, and he had done well. There had been a good deal of trouble from sepsis in this case.

In answer to Dr. Critchley: He thought that Foerster had split the splenium at the original operation; Pfeiffer had postulated these posterior callosal fibres, and this experience proved the assumption because he had cut where the macular fibres would be. There remained the fact that the macular representation must be very extensive, apart altogether from bilateral representation, because, as far as could be judged, the whole of this boy's visual cortex was removed, and the result was preservation of the macula.

The other point concerned the small size of the macula, which should convey a lesson to those who talked about macular vision.

Dr. WILFRED HARRIS said that two days previously he had seen a case of posterior cerebral thrombosis with complete anaesthesia and hemianopia, in a man aged 75, who had had some thrombotic attack. His mentality was good. He (the speaker) had examined the visual fields accurately. He had always been interested in the representation of the macula in the brain. This patient had a split macula. On the other hand, in cases of transient hemianopia due to irritation from a cyst, or a lesion in the neighbourhood of the half-vision centre, the hemianopia lasted twenty-four hours in total degree, without any anaesthesia or hemiplegia, but in these cases also the hemianopia was complete up to the middle line, splitting the macula. This point seemed to him strongly against the theory of bilateral macular representation.

Traumatic Intracranial Aneurysm.—J. PURDON MARTIN, M.D.

W. S., male, aged 45. In March 1936 he was knocked off his bicycle by a collision with a car. He was unconscious for sixteen hours, then suffered from headache, bruises over the left side of the face, and fractures of the mandible. Immediately on regaining consciousness he was aware of a loud rhythmical swishing sound in the head, which seemed to spread to the left ear. The left eye was closed by swelling, and when this subsided there was persistent diplopia. The left eyelid was oedematous from the onset.

In June 1936 the right eyelid became swollen, and at the same time the bruit became louder and seemed to shift to the right side of the head.

Admitted to hospital in November 1936. On examination a loud systolic bruit could be heard all over the skull, loudest over the eyeballs and temples. There was considerable proptosis on the left side, and slight proptosis on the right. The lids were swollen and the conjunctivæ injected. There was a slight internal squint on the right, and weakness in upward and outward movement of the left eye.

By compressing the left carotid artery the bruit could be abolished; compression of the right carotid had no effect. It was therefore concluded that the patient had an aneurysm, probably at the bend of the carotid, and communicating with the cavernous sinus. It was decided that the best thing to do would be to tie the common carotid. Before this was done compression of the artery was carried out for some hours at a time, by means of a makeshift apparatus, but it was not very successful. On November 26, 1936, Mr. Jefferson tied both internal and external carotid arteries on the left side, and there were no ill-effects. For a day or two the

bruit was abolished; the eyes soon receded a good deal, and much of the cedema round the orbits subsided. After two days, however, the bruit returned, and the eyes began to stand out again. It was thought that the ligature might have slipped. Mr. Jefferson therefore operated again (28.1.37), and this time with much better result. There is a slight bruit to be heard now on both sides, but it is more pronounced on the right side. There is still a little cedema round both orbits, but there is very little diplopia. There is also still some weakness of the external rectus on the left side, and the patient still has headaches and the "swishing" sound in his head, and says that bending his head down makes him feel giddy.

Discussion.—Mr. JEFFERSON said that cases of this kind were very difficult to cure. In his earlier days he used to think that nothing could be easier. He had been convinced that one must tie two arteries; one must tie the external carotid at least—in order to prevent the collateral circulation coming back and spoiling the whole matter—and either the internal or the common carotid as well. The chief authority on this procedure was Rudolph Matas, of New Orleans, and his figures showed 60% of cures, a proportion lower than was recognized by most people.

In this patient, although the trouble had begun on the left side, it appeared secondarily on the other side, which indicated an opening-up of the transverse sinus in the diaphragma sellæ, or further back than that. There were evidently not two aneurysms (one on each side) because compression on the right side had no effect, whereas pressure on the left side had.

There had been reported two cases of failure after all varieties of carotid ligature, and in those Dandy had made a frontal flap and put a silver clip on the internal carotids above the point of emergence through the dura, so as to cut out the blood flow coming down through the circle of Willis.

Dr. PURDON MARTIN (in reply) said that he and his colleagues were not very optimistic about this case, as the symptoms had become almost the same on both sides; hence, if the bruit was attributable to the aneurysm, the latter was probably receiving blood from the two sides.

Bilateral Primary Optic Atrophy from Glioma of the Optic Nerves.—

DENIS BRINTON, B.M.

J. S., female, aged 7.

History.—For the last four years she has attended the Royal London Ophthalmic Hospital on account of poor sight. At school, where she has been since the age of 4½, it has always been noticed that she has not seen the blackboard clearly.

Ten months ago she had the first of many fits, which have continued to the present time. The longest interval of freedom was not more than two days. There has been no warning except with the first, when she was twice sick and complained of headache some hours earlier; she seemed "delirious" on that occasion. All other fits have had an abrupt onset. She does not always fall; both arms and legs jerk a little, and the left arm is often raised above the head. She has had incontinence of urine but never tongue-biting. No attack has lasted more than a few minutes, but it may be half an hour before she is normal again; brief frontal headache is the only sequel. No headaches apart from the fits.

On examination.—Bilateral primary optic atrophy, with probable visual acuity of about $\frac{2}{60}$ in each eye. The fields show considerable peripheral constriction, particularly in the temporal halves. Numerous café-au-lait spots over the trunk,

Routine tests of blood and cerebrospinal fluid made at Hackney Hospital in Spring 1936, and at the National Hospital in December 1936, produced entirely normal findings. X-ray examination of the skull in the usual positions showed no abnormality on each occasion, but special views of the optic foramina, taken at the National Hospital in January 1937, showed that each was much larger than normal for the patient's age.

The child is mentally normal except for being somewhat mischievous, but she is obviously suffering from lack of education in a general way because of her poor

vision. Her case caused some difficulty in diagnosis, until special skiagrams of the optic foramina were taken. The normal diameter of the foramina is on an average from 4 to 5 mm., and this, surprisingly, varies very little at differing age-periods. The skiagrams of the foramina in this case show that the foramina are much enlarged, the right measuring 7×5 mm., and the left 6×5 mm. Although these gliomata involve the chiasma and spread forward into the optic nerves from that point, any bitemporal or other sector field defect is unusual.

These cases are not very common. In a series of 170 cases of interpeduncular tumour, from Cushing's clinic, reviewed by Deery in 1930 there were only 14 cases (8%) of gliomata of the optic chiasma—having an average age of 14 years. Three of them had generalized neurofibromatosis. Practically all such tumours are of the type called spongioblastoma polare and this again is relatively uncommon, probably representing about 4% of all the gliomata. These are very slow-growing tumours, almost limited to childhood and are the most common gliomata of the optic chiasma. Its association with von Recklinghausen's disease is undoubted. The only treatment is by radiotherapy.

Discussion.—Dr. PURDON MARTIN said that he was surprised to hear Dr. Brinton quote figures suggesting that glioma of the optic chiasma constituted 4% of all gliomata. He (the speaker) had seen very few cases of the kind, and they were difficult of recognition. The new technique would probably prove a great help in the diagnosis. All the cases of the kind which he had seen, with one exception, had been associated with signs of von Recklinghausen's disease, and in the present case the pigmentation probably indicated a similar association. His experience had been that these patients usually had multiple scotomata, of irregular character, with an irregular contraction of the visual fields.

Dr. ANTHONY FEILING asked what view Dr. Brinton took concerning the nature of the fits in this case, and whether he connected them causally with the glioma.

Dr. BRINTON (in reply) said that a possible interpretation of the case was that the glioma of the chiasma and optic nerves was part of a tuberose sclerosis. There was no obvious mental deterioration, however, to support this, and the fits might more easily be accounted for in other ways.

Mr. JEFFERSON said that his colleagues and himself had done a good deal of work on optic nerve foramina; it had begun over a case similar to the present one—that of a girl aged 12, admitted to hospital because she had burned her hand when falling in a fit. She had been blind on the right side since she was 2 years old, and had an enormous dilatation of the right optic foramen. After being in hospital five weeks she died. There was a spongioblastoma of the optic chiasma, extending back into the subthalamic region, and there was a cyst growing up about the subthalamic nucleus. There was athetosis of the left arm. Knowing the association of meningiomata with von Recklinghausen's disease it was natural to think that in that case they were sheath meningiomata, i.e. of the optic-nerve sheath, but in the only case of that kind which he had had, showing a dilatation of the optic canal, the patient was not the subject of von Recklinghausen's disease. The others he had seen were spongioblastomas, and of 6 patients two had Recklinghausen's disease. When one saw a canal like that in this case one could be sure there was a glioma of the optic nerve.

Dr. W. deG. MAHONEY asked whether a hollowing-out of the sulcus chiasmatis had occurred, giving the sella turcica a boat-like appearance. Also, was there any polydipsia?

Mr. JEFFERSON (in reply) said that the hollowing out spoken of was present in the first case, but it was apparent in Cushing's paper that the foramina were never X-rayed.

He (Mr. Jefferson) had nearly slipped in regard to one case, that of a boy sent from Yorkshire with a six-year history of progressive blindness and bilateral atrophy, and a large sella turcica. He had operated under the idea that there was a cyst, and had come down on a mobile avascular tumour, which he thought it would be well to remove. When he began to mobilize it, the fact dawned upon him that it was optic nerve; he recognized this in time to prevent damage. Cushing had removed an optic chiasma and both optic nerves; his patient did not survive.

Mild Eunuchoid Giantism.--D. E. DENNY-BROWN, M.B.

A. H. aged 19, a tailor.

Family history.—Father short in stature but well developed. Mother of moderate build, healthy. One sister and one brother, both normally developed.

Past history.—Measles when aged 2 years. No history of mumps. A little backward in walking, which he learnt at the age of 2, and in talking; he was of average attainment at school. He has always been shorter than children of the same age, and until two years ago was short and under-developed. He was then 4 ft. 2 in. in height. In the last two years his hands and feet have increased in size rapidly. His size in shoes has increased from 8 to 10. He has grown rapidly in the same period (present height 5 ft. 2 in.) and his head has increased in size. In his work he has noticed difficulty in flexing the fingers during the last two years, and they have become increasingly stiff. He has had no pain and no headache. His vision is not affected. He has never had any facial or axillary hair, and a few sparse pubic hairs have developed only in the last two years. The genitalia have remained under-developed. His voice has not broken.

Secondary sexual characteristics are lacking. The testicles are descended but infantile. The skin is soft and pale. The skull is moderately large, but there is no prognathism. The limbs are strikingly long in proportion to the trunk length. The most remarkable feature is the state of the hands and feet. The fingers and toes are long and tapering, and flexion of the terminal interphalangeal joints is interfered with by a capsular limitation. There is a fusiform swelling of one of these joints, but no other evidence of arthritis. Active epiphysal lines seen in skiagram. Some limitation of full extension of elbows and of lateral deviation of wrists, also capsular. No bony changes in joints seen in skiagram. Absence of usual acromegalic thickening and osteophytes. Sella turcica very small, with thick clinoid processes.

Blood-pressure 100/65 mm.

In the normal course there is an acceleration of growth at this period; is this an enhancement of that acceleration, or is there some further stimulus arising from the anterior lobe of the pituitary? Can the present rate of growth be controlled? With his eunuchoidism, and the delayed closure of epiphyses which accompanies that condition, the ultimate state would seem to be, inevitably, grotesque giantism.

Discussion.—Dr. F. PARKES WEBER said that the case seemed to him more like arachnodactylia; the flat sternum and the contour of the front of the chest favoured that view, but, above all, the long fingers and long toes. He assumed that there were no signs in the eyes suggesting arachnodactylia, such as ectopia of the lens or asymmetry in the iris colour.

Dr. H. S. LE MARQUAND said that this case corresponded closely to those described by Engelbach¹ as primary hypogonadism. He (the speaker) had had several cases under observation. In these cases the pituitary and thyroid growth hormones were normal, but there was a delay in the uniting of the epiphyses, owing to gonadal hormone deficiency. This led to a marked disproportion in the lower measurement, i.e. from the pubes to the sole of the foot, composed of long bones, in comparison with the upper measurement, i.e. from the pubes to the crown of the head, composed of flat bones. They showed genitalia abnormal in function and sometimes in structure; erections and emissions were infrequent or absent; there was a lack of hair on the pubes and in the axillæ, and shaving was infrequent. The head measurement was small and the chin receding. The condition also occurred in girls, in whom the diagnosis was not usually made, as the defect of genital function and structure was not so obvious. The onset of menstruation was delayed and could be initiated by treatment. He had treated both male and female cases with injections of antuitrin S. (Sex)—with benefit in some of them. These cases were usually referred to general hospitals on account of nervousness or some other mental symptom, the gonadal defect having been overlooked.

Dr. R. M. STEWART said he did not think that this patient's phalanges were unduly long or slender, nor were additional epiphyses present, and therefore he would exclude arachnodactylia.

¹ Engelbach, "Endocrine Medicine", 3, p 140.

Mr. ARNOLD SORSBY drew attention to a familial group recently reported by Cockayne in which long limbs, such as those of this patient, were associated with dwarfism, deaf-mutism and retinitis pigmentosa. (*Arch. Dis. in Child.*, 1936.)

Wilson's Disease with Kayser-Fleischer Ring.—M. J. MCARDLE, M.B.

D. B., female, aged 17. Admitted to the National Hospital under Dr. F. M. R. Walshe.

History.—For the past three years has had an increasing tremor of the right hand and arm, and for one year tremor of the left arm also. Speech has been slow, and, at times, indistinct, for over a year. When aged 10 she had difficulty in walking; this lasted about two years, and was attributed to frequent knife-like "rheumatic" pains in the right leg. These occurred daily for three years, but are now less common; they occur rarely in the left leg and right arm. She has always had periodic frontal headaches, and, recently, has had attacks of vomiting with or without headache. Had attacks of giddiness a year ago. Was backward at school; left school at age of 12. Is restless, timid, and sometimes irritable. Nocturnal enuresis from the age of 10 till recently.

On examination.—Vacant expression; some facial rigidity. Backward and childish; memory fair; cheerful; no insight. Speech slow, syllabic, and monotonous.

Kayser-Fleischer ring present as a ring of golden-brown pigment near the limbus of the cornea, most dense in the upper and lower parts, and gradually fading off towards the centre. With the slit-lamp the pigment is seen to be in the posterior layer of the cornea; the ring is about 5 mm. wide, and begins 1 mm. from the corneal margin.

Cranial nerves normal, except for slight lower right facial weakness and some weakness in closure of both eyes. Coarse rhythmic tremor of right hand and arm; absent when arm is at rest; increased by attention or voluntary movement. Similar, but less noticeable, tremor in left hand. Occasional tremor of head. Some rigidity, of Parkinsonian type, in arms and legs; early flexor contracture of right knee. Slight general weakness. Reflexes all normal. No sensory loss. Liver not felt; spleen palpable $\frac{1}{2}$ in. below costal margin on deep inspiration.

Cerebrospinal fluid: Pressure 135 mm. 1 cell. Protein 0.120%. Pandy positive; Lange 0011220000. Wassermann negative in C.S.F. and blood. Lævulose tolerance tests: Normal.

Family history.—Mother normal. Father "nervous and irritable"; his grandfather died in an asylum, and his sister was in an asylum for eight years.

Patient's elder brother died in an asylum, at the age of 16. He was examined here at the age of 12. He had a vacant expression, and lay with his mouth open dribbling saliva. There was considerable mental retardation, and his speech was monotonous, slurred and indistinct. The right side of the mouth drooped slightly, and both eyelids were weak. The right thumb was adducted and the fingers a little flexed. Tone was slightly increased in the right arm. There was some tremor of the right hand and slight weakness of the right arm. Reflexes normal. No sensory loss. Some difficulty in walking. Liver just palpable; spleen not felt. Blood Wassermann reaction was positive. Cerebrospinal fluid: Protein 0.06%. Pandy, weakly positive. Lange, no change. Wassermann reaction negative. A photograph of this boy at the age of 15 is highly suggestive of Wilson's disease. At autopsy the brain showed considerable atrophy of the basal nuclei on the left side. The aorta showed syphilitic aortitis. The liver was cirrhotic, and the spleen fibrous, weighing 16½ oz. Cause of death certified as juvenile G.P.I.

There are three other sisters, aged 12, 5 and 3. The one of 12 is backward mentally, but shows no Kayser-Fleischer ring or other signs of Wilson's disease. The other two appear normal.

The mother's blood Wassermann reaction was negative.

Section of the History of Medicine

President—E. W. GOODALL, O.B.E., M.D.

[February 3, 1937, continued]

The Scientist's Playground

By W. H. S. JONES, Litt.D.

FOR forty years I have studied the history of medicine and of science and philosophy in general, especially that part of it which culminated in the work of Galen. From the very first I have been puzzled and perplexed by certain aspects of the doctrines propounded by many, perhaps most, of the thinkers of antiquity. It is not that these doctrines are particularly abstruse or difficult. Their perplexing character lies rather in their strangeness. Coming to the University from a laboratory training at school, and set down to a study of classical antiquity, I was simply bewildered to learn that some ancient physicians of repute held that diseases are caused by excess of air in man's physical make-up; that some ancient physicists declared the whole universe to be composed of water; and that some ancient scientists of the first rank expounded their systems in verse of a mystical and apparently allegorical character. But the breaking-point came when this bewildered student was told to read the *Timaeus* of Plato. Plato, one knew, was eaten up with his zeal for truth and his passionate yearning for reality, and the *Timaeus* was the work of Plato most valued in antiquity. Here, if anywhere, the student might hope to find something that appealed to the modern mind, and to modern ways of thinking. But he is bitterly disappointed when he reads this *chef d'œuvre* to discover that it contains nothing that could possibly be called science in the modern sense of that word. It consists of two parts:—

(1) The first dogmatically states that the Artificer of the world built it out of space by impressing space with the regular solid geometric figures, thus forming the four "elements"—fire, air, water, earth.

(2) The second part gives a detailed physiology of the human body, highly fanciful yet dogmatic, evidently written by one who had but slight acquaintance with human anatomy. Many diseases are attributed to excess of one or other of the four so-called "elements".

How did Plato reach these strange conclusions? Did he attempt to prove them? What use did he make of them? Nobody seems ready to give an answer, except that he borrowed them from other thinkers.

Again, in the Hippocratic Collection, in the midst of much that, if not scientific in the strict modern sense, is at least full of the truly scientific spirit, we come across whole treatises which are as fanciful as Plato's *Timaeus* or even more so. Examples are the *περὶ φύσων*, which attributes all diseases to irregularities of "airs", either within or without the body, and *Nutriments*, which in language closely following the obscure, oracular language of the philosopher Heracleitus (500 B.C.) explains, save the mark! the process of digestion by comparing it to the "road up and down" of Heracleitus, the said road being the passage of earth through water and mist to fire, as exemplified by the sea-bed, the sea itself, cloud, and finally the sun. All this, mind, we are asked to appreciate, to criticize and to understand from the same standpoint as that from which we view Baglivi's dissociation of typhoid ("mesenteric") from other fevers, or the discovery of vaccination as prophylaxis

against smallpox. That is to say, interpreters of ancient science assume that the ancients were always animated by the same motives as influence a modern researcher, and that the difference between ancient and modern is *always* one of degree and not of quality or essence.

I venture to deny this assumption, and to maintain that some—*some*, not all—of the work done by ancient scientists belongs to an entirely different category from the work done in a laboratory to-day. The objects, the motives, are altogether different, and until this truth is realized, ancient science, and perhaps mediæval science, can never be understood.

I was led to this conclusion by beginning to study a papyrus in the British Museum, the *Anonymus Londinensis*, discovered in 1892, which is not yet well known to English scholars. A great part of it consists of extracts from a History of Medicine made by Aristotle with the help of one Menon, who, as we should say, “devilled” for him. This work is in fact the earliest extant history of medical science, written under the guidance of the most scientific mind of the ancient world. Surely we might expect to find in it something that appeals to a modern physician as being akin and germane to his work and studies.

But a bitter disappointment awaits the reader who approaches the *Anonymus* papyrus with that hope in his mind. The writer deals solely with the aetiology of disease, and is interested in two classes of medical students only:—

(1) Those who attribute diseases to various *περισσώματα*, superfluities or residues of diet;

(2) Those who attribute diseases to irregularities of the blending of the “elements” (earth, water, &c.) of which the body is composed.

There is not a word about the method by which the theories put forward were reached, nor is it stated by what arguments they were defended—if they *were* defended—nor yet what use was made of them—if *any* use could possibly be made, which is more than doubtful.

The whole of the papyrus belongs, in fact, to that region of mental activity that I call the scientist’s playground, to which also must be assigned a great deal of all scientific and philosophic discussion in ancient—and perhaps mediæval—times. For the present I will limit myself to Greek medicine. The Greek doctor had a medical practice differing little in essentials from ours. This practice was based upon a theory strictly scientific in the modern sense. But besides his medical practice, and the simple theory that governed his practice, the Greek physician liked, in the sphere of his own subject, to play a game. He liked at times, not to test his theories by reality, but to *escape* from reality, and to exercise his intellect unfettered by the hard facts of a workaday world. Like the household drudge, who escapes from her narrow environment and seeks in the cinema or music-hall the romance that is denied her in real life, like the bank clerk who seeks relief from his ledgers and balances in detective fiction and thrillers, the Greek physician tried to find recreation by speculating and dogmatizing about medicine. He had no fiction, or at any rate very little, and he had no cinema. He saw no reason why his own subject should not provide him with the means of satisfying this imperious and universal instinct to escape for a time from the world of “what is” to the world of “what might be”—from actuality to possibility. He does not tell us when he ceases to be a severe scientist and begins to be a romancer. He saw no necessity to do this, for he assumed that his reader would exercise common-sense. There is also, as might have been expected, a wide region where fact and fancy blend together, and are hard to keep distinct. But this is not to be wondered at, and does not affect the general truth of my contention.

The game of the Greek physician had its rules; his imagination was not entirely untrammelled. He must observe the laws of logic and of possibility. He must construct a system neither impossible nor absurd, nor yet a fairy story. His account

must be, in the language of the little girl in the anecdote, a *true* story if not a *really* true story. In other words, it must conform to the rules governing the construction of a good novel. Being a Greek the Hippocratic physician felt that his theory must be æsthetically sound, and follow the laws of truth if not of sober fact.

The dangers of this type of speculation are obvious, and did not escape the notice of acute observers. The writer of *Ancient Medicine*, a treatise in the Hippocratic Collection, to be dated about 420 B.C., fiercely attacks all such theorizing in the sphere of medicine. Its proper place, he urges, is in discussing such topics as Heaven and Hell—which curiously enough *did* form the intellectual playground of the mediæval theologian.

The writer, be it noticed, is *not* angry with speculation in general. What he attacks is the direct application of such speculation to medical practice. So to apply it was not playing the game. Speculation was in one sphere—in a sense divorced from reality—practice was in another. It is when the two spheres are confused that danger arises. But this game, this playing with hypothesis and speculation, had, and still has, its value and use. There can be no doubt that the individual mind, as well as that collective mind we call the history of thought, has profited greatly by the habit of rational guessing, which seems to make the intelligence more supple, more alive, better able to deal with likely solutions when all the unlikely have been weeded out by the application of logical reasoning.

I may remark in passing that I find my own problems, whether in my work or in my life, are often made easier of solution if hypotheses are freely suggested, by myself or my friends, about the matter in hand, without at first any effort to test them by references to known facts.

Rational guesses have often proved the forerunners of important scientific discoveries. In the middle of the Vth century B.C. a philosopher-poet and medicine-man—Empedocles—propounded many of those playful hypotheses that puzzled me very much when, as a young man, I tried to interpret them in the way my teachers wished me to do. One of these guesses I wish to discuss more fully.

Empedocles (quoted by Aristotle *De anima* 410a) said that bone was composed out of three of the four so-called "elements" in the following proportions. Of a total of eight parts there were two parts of water, two of earth, and four of fire. One wonders what reply an opponent would have received from Empedocles, if the dogma had been attacked on the ground that the proportions of the elements were incorrect, or that a different group of elements should have been chosen, or that the so-called elements were not elemental. The arguments urged on either side would surely not have satisfied the scientific instincts of a modern thinker. My own reaction to the theory of Empedocles forty years ago was "what rubbish".

But I can imagine Empedocles replying: "I cannot prove my hypothesis in the same way that one can prove that triangles with equal sides have equal angles, or that large quantities of cheese quickly eaten will cause indigestion. I am merely putting forward a suggestion. And though I cannot prove it, I can at least say this, that it is reasonable, consistent with the rest of my theory, and in itself a neat and rather pretty idea. I am convinced that it enshrines a scientific truth of some sort." Had Empedocles so answered he would have been a true prophet. For surely his guess is a brilliant anticipation of chemical formulæ. Of seven parts, sulphuric acid has two of hydrogen, one of sulphur, and four of oxygen.

The same medicine-man, we know not on what evidence (if any), formulated a theory of the evolution of species by the survival of the individuals fittest to cope with their environment. It is crudely, laughably, expressed. In the early ages of the world, says Empedocles, arms and legs wandered about until they met suitable shoulders, eyes, and other limbs, so as to make an organism adapted to its environment. Absurd and laughable, perhaps, but the general resemblance of this playful speculation to the doctrines of Wallace and Darwin is unmistakable.

Again, the wild hypotheses about air and breaths, which I mentioned just now, what are they but the tentative thoughts which ultimately led to the discovery of the part played by oxygen in supporting life?

But I am not concerned with the dangers of misplaced speculation, or with the evolution of scientific truth from wild but lucky guesses. About such things we ourselves can but wildly guess and speculate. My object is simply to point to the importance of remembering, when we try to interpret the history of science, that a strictly scientific criterion is often unfair to ancient thinkers. Science and fiction, in the earliest days of science, were not severely separated one from the other. Reluctance to go a step further than is warranted by observed facts is a principle of comparatively modern origin. In the uncharted region of knowledge the ancient thinker refused to be content with a confession of ignorance. If he could not work in this region he insisted on playing. When he could not be a serious researcher, he felt justified in enjoying a game—an organized game it is true, a game with rules and regulations, but nevertheless a game. And so we find in all ancient thought a curious mixture—theology is blended with legend, history with romance, chemistry with alchemy astronomy with astrology.

My own studies have been chiefly concerned with Greek science, but what I say applies generally to every time and place before the rise of modern science. To understand Greek medicine we must understand the Greek mentality. We cannot be good interpreters of ancient medicine so long as we are slaves of the modern spirit. We must attune our minds—and our hearts—to the spirit of antiquity. We must try to recapture something of its freedom, its gaiety and its playfulness. The Greek physician could be—as Hippocrates was when he wrote his clinical histories—severe enough and austere enough to satisfy the most exacting of modern critics. But at other times, even when occupied with a technical subject, he threw off his spirit of seriousness. He became an irresponsible child, a romping schoolboy revelling in the unfettered exercise of active and growing limbs. This exercise was his chief intellectual recreation, and there might be worse recreations.

But how can we tell when he is serious and when he is playing? How can fact be separated from fancy? Only by earnest and, above all, sympathetic research. Sometimes we are in no uncertainty, for the truth is obvious. But there are occasions when science and fiction combine in a twilight of dubiety, and we are left intellectually puzzled, but amazed at the fertile imagination of a people who, whatever their failings, never forgot that truth, besides being true, is always, although we cannot always see it, harmonious and beautiful.

Section of Surgery

President—G. GREY TURNER, M.S.

[February 3, 1937]

DISCUSSION ON INJURIES OF PERIPHERAL NERVES

Mr. Harry Platt

NEARLY twenty years have passed since the heyday of peripheral nerve surgery, and a generation of surgeons now exists which had no share in the unique experience afforded by the reconstructive surgery of the Great War. In going through some old operation lists, I am reminded that in the month of February 1920, I explored 41 injured nerve-trunks. A year later, in my Hunterian Lectures at the Royal College of Surgeons, I was able to present an analysis of the pathological findings in 510 peripheral nerve operations done between March 1915 and December 1920.

The conditions of civil surgical practice provide no such comparable wealth of material. The contrast is most chastening. Thus, during the past six years (1931-1936 inclusive) I find that my own experience in this field has comprised the modest total of 89 operations collected from my hospital and private records (Tables I and II).

TABLE I.

	Exploration. No lesion, or repair abandoned	Suture	Neurolysis	Suture and neurolysis	Anterior transposition	Total
Brachial plexus	3	1	4	1	—	9
Median nerve	—	9	6	—	—	15
Ulnar nerve	—	13	6	—	36	55
Musculospiral	—	1	3	—	—	4
External popliteal	—	3	2	—	—	5
Anterior tibial	—	1	—	—	—	1
	3	28	21	1	36	89

TABLE II.—CLINICAL TYPES OF NERVE INJURY IN THE OPERATION SERIES
IN TABLE I.

I. Nerve injuries complicating fractures and dislocations	...	39
II. Nerve injuries due to penetrating wounds	—	32
III. Traction injuries of the brachial plexus	...	9
IV. Nerve injuries due to miscellaneous causes	...	9
Median neuritis due to intravenous injection	...	1
Ulnar neuritis due to	<div style="display: inline-block; vertical-align: middle;"> <div style="display: inline-block; vertical-align: middle; font-size: 2em;">{</div> <div style="display: inline-block; vertical-align: middle;"> hypermobility ... osteo-arthritis of elbow ... internal derangement of elbow ... epicondylar bursitis ... </div> </div>	1 2 4 1
Total operations	...	89

In three cases the median and ulnar nerves were explored at the same operation.

It must, of course, be remembered that a considerable proportion of the nerve injuries of civil life do not reach the operating theatre. This applies more especially to many of the lesions associated with fractures, and to the great majority of traction lesions of the brachial plexus both in the infant and in the adult. The series quoted above (Tables I and II) represents on the whole the more severe types of nerve-lesion, in which some form of operative repair has been considered necessary. It will be seen that the series does not cover the complete repertoire of peripheral nerve operations. In the first place there are no operations for facial palsy, the treatment of which lies outside my special field. I have also omitted from the series the few cervical rib operations which I have done during the same period. With these reservations, the 89 operations may be regarded as fairly representative of the field of peripheral nerve surgery.

Clinical types of nerve injury.—The nerve lesions of civil practice are produced by a variety of causes, and in consequence the clinical problems thus presented differ very widely. I propose to confine my attention to three clinical groups.

[GROUP I.—NERVE INJURIES ACCOMPANYING FRACTURES AND DISLOCATIONS

In the compound injuries of warfare, and to a lesser extent in the corresponding injuries of civil life, the coincidence of a fracture and a nerve lesion excites little surprise. In simple fractures, peripheral nerve complications are uncommon, and when they occur, may appear somewhat unexpectedly. The signs of nerve involvement not infrequently become fully established only during the early weeks following the injury. In such circumstances the methods used in treatment of the fracture may be open to serious criticism. The subject of dual injuries is far too extensive to be discussed in great detail. I have therefore selected a number of clinical types which illustrate the more important factors concerned in prognosis and treatment.

(1) *Dislocations and Fracture-dislocations of the Shoulder-joint*

Apart from circumflex palsy nerve complications in dislocations and fracture-dislocations of the shoulder are undoubtedly rare. Although it is well known that clumsy and unskilful manipulation during attempts at reduction may be responsible for such complications, the nerve-lesions encountered in actual practice are usually unavoidable.

(i) *Circumflex palsy* is seen in about 5% of all subcoracoid dislocations reduced promptly and efficiently in the ordinary routine of a large casualty department and fracture clinic. The nerve-lesion is a traction injury produced simultaneously with the dislocation. As the head of the humerus is thrust downwards towards the axilla the nerve is suddenly over-stretched but is rarely, if ever, completely ruptured. In the majority of the circumflex lesions, with appropriate relaxation and re-education complete recovery from the resulting deltoid palsy takes place within three or four months. Even the slighter forms of deltoid paresis prolong the incapacity period far beyond that of the ordinary shoulder-joint dislocation—a consideration of economic importance. In exceptional cases incomplete recovery in the deltoid may be seen after many months of treatment. Total and permanent paralysis of the deltoid, indicating complete rupture of the nerve, is fortunately almost unknown, and, for practical purposes, such a lesion must be regarded as beyond repair.

(ii) *Infraclavicular plexus trunk involvement.*—It is generally taught that damage to one or more of the infraclavicular plexus trunks may be sustained either at the time of the dislocation (a primary lesion), or may develop later in an unreduced dislocation or fracture-dislocation of some days' or weeks' standing (a secondary lesion). In my own experience of this complication I have found that the nerve-lesions almost invariably date from the moment of the joint injury, and that when the nerve-trunks have escaped initial damage the continued presence of the dislocated head in the axilla does not necessarily, or even commonly, set up a compression neuritis. I have also been impressed by the association of comparatively serious nerve-lesions with dislocations which presented no difficulty in reduction.

The full effects of a severe infraclavicular plexus lesion are rarely demonstrable during the first week. The more spectacular wrist-drop not infrequently masks, for a time, a co-existing palsy of the intrinsic muscles of the hand. Of the three secondary plexus trunks—the outer, inner, and posterior cords—the first most often escapes injury. The typical clinical picture in the early stages usually indicates the presence of (a) a combined lesion of both posterior and inner cords, or (b) a lesion limited either to the inner or to the posterior cord. A posterior cord lesion is rarely overlooked, for the complete syndrome consists of a palsy of the deltoid, triceps, and extensor muscles of the forearm. An inner cord lesion is recognized by its crippling effects

on the hand—palsy of the intrinsic muscles (both median and ulnar supply), rigid clawing of the fingers, and the trophic changes characteristic of an irritative nerve-lesion. In addition there is a sensory loss in the ulnar area of the hand and the post-axial half of the forearm.

The prognosis in *primary* lesions of the infraclavicular plexus trunks is not, on the whole, unfavourable. In posterior cord lesions complete recovery within periods of three to six months is the rule. The recovery time for the inner cord is much more prolonged, and in the majority of cases recovery always proves to be incomplete. But in spite of the persistence of some degree of intrinsic palsy, sensory loss, and contracture of the fingers, in a small group of patients examined some years after the injury I have been surprised to find very useful working hands. This experience of the results of conservative treatment has persuaded me that no advantage is to be gained from an exploration of the injured nerve-trunks in the early stage.

In the true *secondary* lesions associated with an unreduced dislocation spontaneous recovery always tends to be inhibited owing to the strangling effects of the extensive scar-tissue which forms round the dislocated head. In such circumstances, I hold that the nerve-trunks should be freed without delay, either by an open reduction or by excision of the head of the humerus.

(2) *Musculospiral Lesions in Fractures of the Humerus*

Although the musculospiral nerve is most intimately related to the shaft of the humerus in its middle third, musculospiral palsy in fractures at this level is an infrequent complication. In my own fracture clinics the incidence is about 5%. In birth fractures of the humerus it is interesting to observe that a transitory wrist-drop is by no means an uncommon phenomenon.

Musculospiral palsy may be seen either as a primary or as a secondary lesion. *Primary* lesions usually result from the direct impact of a bony fragment, and may easily be produced by over-zealous and quite superfluous efforts to manipulate the fracture into mathematical alignment. *Secondary* lesions are due to the adherence of the nerve-trunk to a projecting fragment or irregular bony surface, and not to actual enclosure of the nerve in callus—as usually taught. In such surroundings the nerve-trunk, though at first intact, becomes gradually obliterated by dense cicatricial tissue.

Experience has shown that the majority of musculospiral lesions accompanying simple fractures are capable of undergoing spontaneous recovery. For this reason, it is sound practice to employ conservative methods of treatment over a period of three to four months. This applies more especially to the secondary lesions. If, after such a probationary period, the signs of a complete block still exist, the nerve should then be explored. In primary injuries it is justifiable to explore at an earlier date, if the radiographic findings suggest the existence of a grave lesion.

Of the four operations on the musculospiral nerve included in my latest series (Table I), the one suture operation was a delayed repair of a complete anatomical lesion accompanying a compound fracture. The operation was carried out four months from the date of the injury, and two years later complete restoration of power in all muscles of the extensor group had taken place. The three neurolysis operations performed for incomplete lesions showing failure of recovery after four months' conservative treatment were followed by rapid return of function. These results are, of course, what past experience has led us to expect from the musculospiral nerve.

In civil practice massive destruction of this nerve, with the production of a gap too wide to be bridged, is very rare. In a period of twenty-three years I have had only two examples of such irreparable lesions. In both cases the classical tendon transplantation, used with such brilliant success for irreparable gunshot injuries, restored the lost function of extension of the wrist and digits.

(3) *Nerve-lesions in Fractures and Dislocations of the Elbow*

Although the elbow provides the majority of the dual injuries of bone and nerve, the incidence of nerve complications in fractures and dislocations in this region is, in actual fact, very low. The nerve-lesions in this group are almost exclusively seen in conjunction with fractures of the lower end of the humerus or subluxations of the elbow-joint. In fractures of the olecranon and upper end of the radius peripheral nerve involvement is almost unknown. The circumstances in which the three main nerve-trunks of the upper limb become liable to injury may be briefly reviewed.

(i) *Ulnar lesions*.—The special vulnerability of the ulnar nerve in the post-condylar groove is well recognized. The predominance of ulnar lesions is strikingly illustrated in the operation series in Table I. The lesions are invariably incomplete and in the majority of cases recover spontaneously under conservative treatment. In a minority the clinical picture of a severe progressive neuritis becomes established. For this, the special type of neurolysis operation involving transposition of the nerve to the front of the elbow, is demanded. The factors concerned in the production of the nerve-lesions are most conveniently studied from a chronological standpoint. In this connexion three clinical types are usually distinguished—(a) primary, (b) secondary, and (c) tardy lesions.

(a) Primary lesions occur most frequently in association with traction fractures of the *internal epicondyle*, the nerve being contused or stretched during forcible abduction of the forearm. A similar injury may occasionally accompany a *supraco-dylar* fracture. In the ordinary type of epicondylar fracture with little or no displacement of the detached fragment the ulnar lesions are generally mild and recover completely without special treatment in a few weeks. A more severe form of traumatic neuritis is liable to be induced when the internal epicondyle is torn off as part of a subluxation or complete lateral dislocation of the elbow-joint. In such cases the epicondyle may become wedged in the inner compartment of the joint and for the time being acts as a block to reduction. The already damaged nerve-trunk is then placed under conditions of excessive tension.

Inclusion of the epicondyle in the elbow-joint is a clinical entity which has received considerable attention in recent years. The incidence of this complication is illustrated in the following analysis made by my colleague Osmond Clarke of a series of elbow fractures and dislocations treated in my hospital fracture clinics :—

JANUARY 1929 TO SEPTEMBER 1935 (6½ YEARS PERIOD).				
Fractures	741	Proportion of "epicondyle in joint"		
and		to :—		
Dislocations of elbow	178	(a) Total elbow injuries ...	1 in 42	
	Total 919	(b) Total epicondyle fractures	1 in 8	
Total fractures of internal epicondyle	166	(c) Total dislocations ...	" 1 in 8	
"Epicondyle in joint"	22			

In the 22 examples of epicondylar inclusion the ulnar nerve showed evidence of primary damage in 17. In these the injured nerve was explored and transposed. The majority of the operations were done during the first forty-eight hours as, in addition to the exposure of the nerve, it was necessary to extract the epicondyle from the joint. In two cases it was found that the nerve-trunk had entered the joint with the epicondyle.

In the epicondylar inclusions treated in my fracture clinics during the past eighteen months the earlier recognition of this complication has made possible the more frequent replacement of the fragment by manipulation alone. Where manipulation has been successful it is an advantage to delay operation on the nerve for the following reasons : (1) The probability that the milder lesions may undergo spon-

taneous recovery. (2) Owing to the extensive tearing of the common flexor muscle mass, it is difficult at this stage to provide an ideal intramuscular bed on the front of the elbow.

(b) Secondary lesions make their presence known some three or four weeks after the time of injury, and may be seen both in internal epicondylar and supracondylar fractures. The underlying cause is a disturbance of the normal relation between the nerve-trunk and its bed. Distortion of the post-condylar groove is usually the result of failure to replace a detached epicondyle or to correct lateral displacement of the lower fragment in a supracondylar fracture. In such circumstances the nerve-trunk becomes less mobile, takes a slightly longer course, and becomes liable to over-stretching in energetic movements of flexion of the elbow-joint. These are the conditions which favour the onset of a friction neuritis. The use of forcible movements at this stage, whether active or passive, may be disastrous. In actual experience it has been found that the majority of secondary ulnar lesions have been precipitated by incompetent treatment of this kind.

In the mild forms of secondary neuritis recovery begins as soon as the elbow is put completely at rest. In the severe lesions anterior transposition of the nerve is necessary.

(c) Tardy lesions.—The syndrome of late ulnar palsy calls for no detailed description. It is sufficient to remember the three phases of the clinical picture: (a) A fracture of the external condyle in early childhood, which fails to unite, followed by the development of a cubitus valgus deformity; (b) a latent period which may extend over many years; (c) the insidious onset of the signs of ulnar neuritis in later life. It is in this special form of friction neuritis that the operation of anterior transposition has achieved some of its outstanding successes.

(ii) *Median lesions*.—Owing to its more protected situation the median nerve is rarely implicated in elbow-joint fractures. The nerve-trunk is, however, occasionally impaled on the projecting lower end of the shaft in a supracondylar fracture with gross backward displacement of the lower fragment. Such primary lesions have, in my experience, generally been incomplete, and where the displacement has remained uncorrected the integrity of the nerve-trunk has been further jeopardized by scar-tissue strangulation. I have also seen additional injury result from unskilful manipulation in attempts to reduce the fracture and from the premature use of forced movements to hasten return of mobility in the elbow-joint. Median nerve injuries can, therefore, to some extent be prevented, or their gravity minimized, by the efficient handling of supracondylar fractures. In the mild lesions exhibiting a slight degree of nerve-block without irritative signs conservative treatment is sufficient. In the graver lesions early neurolysis is always desirable. The operation involves release of the nerve, trimming-off the bony projection, and the interposition of a muscle-flap or free fascial graft. The remote results of this procedure in my hands, in some half-dozen cases have been most satisfactory.

(iii) *Musculospiral lesions* are most exceptional complications of supracondylar fractures. The factors which may determine implication of this nerve are contusion or laceration by a bony fragment at the time of the fracture, adherence to the site of fracture, and injudicious manipulation of the elbow-joint. The nerve-lesion is treated in accordance with general principles.

(4) *External Popliteal Lesions in Ligamentous Ruptures of the Knee-joint* (Fractures of the Styloid Process of the Fibula).

In extensive ruptures of the ligamentous structures on the lateral aspect of the knee, produced by powerful adduction of the leg on the thigh, the external popliteal nerve may sustain most serious damage. These injuries are not very common, but during the last fifteen years I have operated on seven cases belonging to this interesting group of nerve-lesions. In two, a complete dislocation

of the knee had been recognized after the accident. In one a delay of two hours before reduction was attempted and resulted in serious arterial block and ultimate gangrene of the toes. The knee-joint in all cases showed the following combination of lesions on the outer side: (a) Avulsion of the biceps tendon from its fibular insertion; (b) detachment of the styloid process of the fibula, with upward displacement of a bony fragment of varying size; (c) a complete tear across the lateral capsule of the knee immediately above the level of the articular margin of the tibia. The external popliteal palsy was recognized in each case within a few days after the injury, and the nerve was explored at intervals varying from two weeks to three years from the date of the accident.

In five cases a complete anatomical lesion with a most extensive gap was discovered, and under conditions of extreme difficulty the operation of end-to-end suture was carried out. Three of the operations were amongst the most difficult nerve repairs that I have ever encountered. The findings were most extraordinary and may be of considerable value for future guidance in cases of this type. In each case, after a prolonged search, the remains of the distal end of the nerve-trunk were disentangled from a block of scar-tissue on the front of the knee at the site of the old tear in the lateral capsule. From this region traces of a fibrous cord could be identified running backwards and upwards to become continuous with the proximal end of the nerve in the lower third of the thigh. It was evident that the nerve-trunk had been actually dragged into the outer compartment of the knee-joint, either at the moment preceding its rupture or immediately afterwards. In one case the wedge of scar-tissue projecting into the joint also contained a bony ossicle representing the fibular styloid. This comparatively rare injury is exactly comparable to the more familiar inclusion of the internal epicondyle in the elbow-joint.

The results of the five suture operations were as follows: (a) *Two* were complete failures and there were no convincing signs of regeneration at the end of three years. One of these belonged to the small group of the three most difficult sutures. (b) *Three* patients showed useful recovery of motor and sensory function. In one, an army officer, the recovery could be described as perfect. This was one of the three difficult sutures, but the nerve repair was carried out ten days from the time of the rupture. An almost complete recovery, judged from a neurological standpoint, was obtained in the remaining difficult suture. In the third case, in which a suture was performed three years after the date of injury, the recovery consisted in the return of feeble power in the anterior tibial muscles, and imperfect return of sensation.

GROUP II.—NERVE INJURIES DUE TO PENETRATING WOUNDS.

In the upper limb injuries of nerve-trunks due to penetration of sharp particles are rarely encountered above the level of the lower third of the forearm. It is a surgical commonplace that division of either the median or the ulnar nerves is often complicated by division of neighbouring flexor tendons. It should constantly be impressed upon hospital casualty officers that either of these important nerves may be completely divided through a tiny wound, and that in all penetrating wounds in the lower half of the forearm a careful test of (a) median and ulnar nerve function, and (b) flexor tendon function, should be made. If this routine were followed, few median injuries, at least, would be overlooked.

There is little to be said about the technique and prognosis of primary and secondary nerve suture for division of the median or ulnar nerves. When the accidental wound is small and appears to be reasonably clean, primary suture may be practised with safety, and an appropriate tendon repair carried out at the same sitting. This procedure was followed in 12 operations in the series in Table I. It is essential that the sutured nerve should be shut off from direct contact with the area of the tendon repair.

In more extensive wounds with widespread bruising and multiple tendon injuries,

and in wounds in which infection has already secured a hold partial or complete failure of regeneration after primary suture is almost inevitable. In such circumstances it is better to postpone repair of the nerve-lesion until the wound conditions are more suitable.

The results of the repair of civil nerve injuries due to penetrating wounds were clearly stated some thirty years ago by Sherren, and more recent experience has added little to our knowledge in this respect. In primary sutures performed under ideal wound conditions complete recovery of motor power, and recovery of protopathic sensibility at least, is to be expected. In secondary sutures partial or complete motor recovery with imperfect restoration of sensation has been the rule.

Nerve injuries in the lower limb following penetrating wounds are rare. One of the external popliteal sutures in the series in Table II was done for a complete section of the nerve produced by the entry of a fragment of glass. A rapid and complete recovery was seen.

GROUP III.—TRACTION LESIONS OF THE BRACHIAL PLEXUS

The plexus lesions in this group present two distinct clinical problems: (1) The traction lesions of the infant sustained during a difficult birth (obstetrical palsy); (2) the traction lesions of the adult (or older child), produced most commonly under the conditions of road accidents.

(1) *Birth Palsy*

The clinical and surgical problems connected with obstetrical palsy have been most carefully studied during the past twenty years, owing to the large amount of material available in hospital clinics. It is well known that the majority of cases show spontaneous recovery of varying degrees in the first few months. In a few recovery takes place rapidly and complete voluntary power returns in the affected muscle groups. Such limbs may ultimately show no blemish of any kind. Imperfect recovery is, however, the rule, with defective growth of the limb, and a tendency to the development of contractures of the shoulder and forearm which in the great majority of birth-palsies are chiefly responsible for the residual disability. The evidence drawn from clinical experience and from a study both of experimental plexus lesions on the cadaver and of operation findings, has persuaded the majority of surgeons called upon to deal with this disability that operations on the plexus have little or nothing to offer. It is true that from time to time exceptional results have been seen following the repair by suture of circumscribed lesions. This has led to the advocacy of more frequent exploration of the plexus. My own views on this question have changed from time to time. In the past twenty-two years some 300 cases of obstetrical palsy have come under my observation. In only 10 of these have I felt impelled to explore the plexus. Of the 10 operations three consisted of the repair of localized lesions, namely, (a) resection and suture of the upper trunk in two cases; (b) a resection and suture of all three supraclavicular trunks in a third case. In the upper-trunk sutures a partial recovery in the function of the upper-arm group of muscles occurred, and in the total plexus repair there was excellent recovery in the upper-arm group, but complete failure of recovery in the lower-arm group. The operations were done on infants under the age of one year, i.e. within the recovery period for plexus lesions, and I am not convinced that they conferred any material benefit on the limb. In the remaining seven operations nerve-trunks, barely recognizable but obviously intact, were disentangled from scar-tissue, or irreparable lesions were disclosed. I am also bound to admit that the effects of the neurolysis in these cases was negligible.

(2) *Traction Lesions in the Adult*

The plexus lesions in the adult tend to be much more severe than those of the newborn infant. In the latter the over-stretching of the nerve-trunks during

delivery is a more gradual process, and the chief damage is often confined to the upper roots or upper trunk at the level of Erb's point. In the special circumstances of road accidents the traction force applied to the plexus is always sudden, and is often immensely powerful. In a considerable number of cases all three nerve-trunks are involved with the lesions concentrated at different levels. Apart from the initial rupture of nerve-fibres the widespread fibrosis which develops within and around the nerve-sheaths effectively blocks the downgrowth of a sufficiency of regenerating axons.

We must admit with reluctance that the majority of these lesions are not amenable to surgical repair, and in a number of cases the lesions are completely inaccessible. But, as in obstetrical palsy, the opportunity occasionally arises for the repair of a circumscribed lesion of one or more trunks. Such a consideration brings up the much-debated question of the rationale of early exploration in the treatment of plexus injuries.

My own experience has convinced me that such a procedure is sometimes justifiable but that its main value lies not in the chances of effecting repair—which will be exceptional—but as an aid to diagnosis of the extent of the lesion. Thus, in one recent plexus operation performed within ten days from the time of the injury I was able to establish the presence of a complete avulsion of both the upper and middle trunks at the level of the intervertebral foramina—i.e. irreparable lesions. This information enabled me to decide that the long period of splinting of the upper limb in abduction, which most adult patients with plexus injuries find extremely irksome, would be a waste of time. We were able then to concentrate on a special programme of physical treatment of the forearm and hand in which considerable recovery of function ultimately occurred.

Late operations on the plexus, where recovery is absent or delayed, are also of very doubtful value, although some improvement may occasionally follow a neurolysis in which the injured nerve-trunks have been *effectively mobilized*. A clean sweep of all perineural scar must be made, and an essential step is the free excision of the fibrous remains of the scalene muscles.

I find that I have operated on 16 of the 70 plexus injuries of which I have detailed records :—

(1) Eleven of the operations were classified as neurolyses, or were explorations which revealed irreparable lesions.

(2) Five were sutures at various levels :—

- | | |
|--------------------------------------|------------------------------|
| (a) Upper trunk (Erb's point). | (c) Upper and middle trunks. |
| (b) Fifth root (above Erb's point). | (d) Lowest trunk. |
| (e) Upper, middle, and lower trunks. | |

In two cases (the suture of the upper trunk, and the suture of the upper and middle trunks) useful recovery was seen in the upper-arm group of muscles at the end of a year. These results are not inspiring, but they suggest that there is a very small group of lesions in which a limited repair may occasionally be of practical value.

Sir Robert Stanton Woods

An electrical examination is of no assistance in the early days following a supposed injury to a peripheral nerve. Were it not for the fact that statements to the contrary are still made, I should not have thought it necessary to emphasize the fact that, even after complete anatomical division of peripheral motor neurones, we cannot expect diagnostic alteration in the electrical behaviour of muscle earlier than about the tenth day.

I would say here quite definitely also that electrical reactions give indications merely of interference with the functions of excitability and conductivity. Even

complete reaction of degeneration conveys no definite indication of the severity of the anatomical lesion or, in my experience, of its nature.

Before attempting an analysis of normal and abnormal action phenomena, as displayed by skeletal muscles when these are stimulated by electrical currents, we ought first to have a clear comprehension of what these phenomena are.

When a normally innervated skeletal muscle contracts as the result of an electrical stimulus, the stimulus is conveyed along motor nerve-fibres to the end-plates, whether the stimulating electrode is applied to the nerve or is placed directly on the muscle itself. The most effective point for the application of the stimulus, therefore, is that area overlying the muscle which corresponds to the entry into it of the motor nerve—the so-called “motor point”. The precise nature of the tissue change which acts as a stimulus has not been determined, but we may, for purpose of argument, assume that this is a sudden displacement, and consequent accumulation, of ions. At any rate, the resulting phenomena would be explicable on these grounds. In order to act as a stimulus, this displacement-accumulation must satisfy two requirements: (1) It must be sufficient in degree, and (2) it must conform to certain time relationships.

Thus, a constant (or direct) current may rise to an intensity far in excess of the liminal intensity for causing a contraction without causing this, if the increase in strength has been a slow one. As we know, during the passage of a current of unvarying intensity no visible contraction occurs. If, now, the current suddenly ceases, provided again that it had attained a sufficient strength, or if there occurs a fall in strength of sufficient depth and rapidity, another contraction occurs. Both these contractions are brisk, i.e. the shortening in length of the muscle is quick and is followed by an almost equally rapid relaxation. A sudden reversal acts in the same way as a break (with an immediately succeeding rise). If these shocks are sufficiently rapidly repeated, the effect is a sustained “tonic” contraction or “tetanus”. A voluntary contraction is a “tetanus”.

Here we have the whole essence of normal responses: (1) The response to the make or break of a direct current is a very rapid contraction succeeded by an equally rapid relaxation. (2) A sustained tetanus during the whole time of exposure to faradic stimulus. (3) The optimum skin point of stimulation is the “motor” point. (Here let me point out the contradiction in terms involved in the expression “brisk faradic response”.)

In what respects do we find deviation from this syndrome? Before proceeding to deal with this question, I should like to state emphatically that characteristic, abnormal responses are found only in connexion with lower motor lesions; upper motor lesions do not provide characteristic responses. The only possible exception to this dogmatic statement is the so-called myasthenic reaction. This I have never been able to demonstrate and, indeed, I have always entertained with regard to it the suspicion that its description has been based upon theory rather than upon observation.

There are three main essentials in which the results of electrical stimuli applied to muscles and nerves, in conditions of injury or disease of lower motor neurones, differ from those just detailed. First, no contraction is produced if the stimulus applied is a faradic one. Secondly, the contraction process which follows upon the make or the break of a direct current, instead of being a quick muscular twitch which occupies a small fraction of a second, occupies an appreciable interval of time, perhaps one second or even longer (“sluggish contraction”). This, in turn, is succeeded by a still more prolonged period during which the contraction is very slow and deliberately subsiding (“sluggish relaxation”). The third point of difference is the phenomenon known as “longitudinal response”—erroneously named “tendon response”. Instead of the “liminal” stimulating site (motor point) being the point of entry of the nerve, this is no longer the case. Frequently it is stated that now the “motor point” has shifted to the tendon; hence the expression “tendon response”. The

facts are that in the reaction of degeneration the earliest contraction, i.e. the contraction produced by the smallest intensity of current, occurs when the whole length of the muscle is included in the current path. The explanation of this longitudinal response is interesting, because it has a bearing also upon the reason for the sluggish nature of the contraction and relaxation following upon direct current stimuli. With the indifferent electrode lying proximally, and the active one on what was the motor point of a now denervated muscle, the stimulus is largely confined to those muscle-fibres which lie between the two electrodes, whereas, with an electrode lying at each end of the muscle, the stimulus is applied to its whole length and therefore a much larger number of muscle-fibres is excited. A similar explanation possibly applies to the sluggish nature of the direct current response. In a healthy muscle-nerve organ the stimulus, wherever applied, is conveyed to all the muscle-fibres by nerve-tissue and therefore practically simultaneously. With a denervated muscle, the fibres, which of course are stimulated directly, probably do not receive the stimulus simultaneously and therefore do not contract simultaneously, thus there is a more sustained contraction and a consequently prolonged relaxation. In all probability, however, the contraction phenomenon in the individual fibre in such a muscle is itself a more sustained or prolonged one, because, when the stage of sluggish contraction has been reached, there is a degree of actual muscle degeneration present.

(So-called "polar reversal" is now hardly ever considered in any discussion of the behaviour of muscle under electrical stimulation.)

At one end of the scale, then, there are normal responses; at the other, the reaction of degeneration. Between these extremes there are many combinations of responses—varying degrees of excitability by faradism down to inexcitability, in different combination with varying degrees of slowness of direct current response. Many efforts have been made to graduate reactions in accordance with the degree of severity of the nerve-lesion. The present situation with regard to such possibility will be understood if we consider the physiological explanation of the syndrome of the reaction of degeneration—a consideration which will also bring to light clinical features of great interest.

Sluggish response and longitudinal response are, in this connexion, merely phenomena to be noted. Being purely qualitative differences, they are, therefore, not likely to lead to quantitative analysis of degree of lesion, although in themselves they are valuable guides. The point of difference between muscles with intact nerve-supply and those without nerve-supply which concerns such an inquiry as that suggested, is their relative behaviour towards faradic and direct current stimulation. The most important experimental work upon this question has been done within the last twenty years; and, in so far as concerns its somewhat limited bearing upon clinical investigation, is largely due to the painstaking research of Dr. Adrian in this country.

The outstanding difference between the faradic and the direct currents, from the point of view of such investigation, is neither the intensity of current which is ultimately attained in applying a stimulus, nor the fact that, whereas one is a simple make or break, the other is a rapidly repeated series of these. From the point of view of stimulating effectiveness, one single alternation of a faradic stimulus has an effect identical with that of a tetanizing current.

The important item of difference lies in the length of time the stimulus lasts or rather, in the duration of the effective strength of the stimulus. As we have already seen, a current to be effective must conform to two requirements. It must (a) attain a certain minimal intensity and (b) conform to certain time relationships. However strong, the current will not excite if its duration falls below a certain minimum; and its strength cannot be reduced below a certain level, however much its duration may be prolonged. For all durations which are long compared with the minimal duration, the strength of current required to excite remains constant at its

minimal value. As the minimal duration is approached, the strength must be increased and the increase becomes more and more rapid as the duration is reduced. These requirements can be expressed in a curve—the strength-duration curve.

The intensity cannot be increased nor can the duration be reduced indefinitely, but for every excitable tissue the excitability can be expressed in such a curve and may be defined by two factors, viz. the *rheobase* and the *chronaxie*. The former name is given to the strength of current required to excite when its duration is infinite; the “*chronaxie*” is the name given to the duration (somewhat arbitrarily chosen) at which the current must be increased to twice its minimal strength or rheobase. The *chronaxie* is constant for the same tissue examined under similar conditions of temperature, &c.; it shows very great variations from one tissue to another. The *chronaxie* of nerve and of muscle is, then, an expression of the electrical excitability of the two tissues with which we are concerned, varying hardly at all from one healthy skeletal muscle to another, but very widely under different conditions of health and degeneration. The *chronaxie* of healthy nerve, or of healthy human muscle with intact nerve, is of the order of $1/10$ ms.; that for muscle whose nerve has degenerated is of the order of 10 ms. [1 ms. = .001 second.]

Now Adrian and others have pointed out that a single element of the faradic current has an effective duration of the order of 1 ms., whereas the duration of a galvanic (or direct) current, when the circuit is made and broken by the hand, is of the order of half a second. The latter stimulus will therefore last long enough to excite both healthy muscles and those with degenerated nerve-supply; whereas the faradic stimulus will excite only those with a comparatively short *chronaxie*—healthy muscle. Can this type of experimentation, so elaborate as to be almost limited to the physiological laboratory, afford any guide to the severity of the lesion or an answer to the question whether the nerve is degenerating or recuperating?

To decide whether electrical testing can help in these respects it is necessary briefly to consider the character of the strength-duration curve for healthy muscle and for muscle whose nerve has degenerated. Put very briefly: The strength-duration curve of healthy muscle is of certain highly characteristic and constant type, whilst that of muscle whose nerve has completely degenerated is equally constant and characteristic, but totally different from the former. Adrian interprets these as being the curves of nerve and muscle respectively (though this view is not universally accepted). He points out that the only essential variation in character from one or other of these two types which is found during the degenerative process or during recovery is a compound curve or rather two curves—one resembling that of nerve (short *chronaxie*) and the other that of muscle (long *chronaxie*); there is never a curve showing a *chronaxie* half way between these two. It is inferred therefore that electrical reactions give evidence of (1) excitable nerve-fibres, and (2) denervated muscle. There is no gradual transition from one type of curve to another, no third type of curve indicating a half-way stage in nerve recovery; and Adrian therefore concludes that electrical reactions must play an extremely subordinate part in prognosis and in diagnosis of severity.

It appears to me that this view greatly underrates the value of his own experimental work and of that of others. At present such methods are too technical and complicated to be clinically practicable. The conclusions, however, make a considerable advance in our understanding of muscle-nerve phenomena. With respect, too, I would venture to suggest that here again is another instance of the necessity for extensive clinical application of what are as yet largely experimental observations.

With regard to statements that an electrical examination elicits few, if any, facts unobtainable by other neurological tests, I entirely disagree. There is, for example, the obvious fact that the only positive proof of the hysterical nature of a paralysis is the muscle-response to electrical stimulus and that, by this means, not only may an hysterical paralysis be definitely proved to be such but, in a paralysed

limb, the organic and the functional can be accurately segregated. Muscle-testing, too, will differentiate between muscles which fail to function owing to pain, and those which are affected by a lower motor lesion. An accurate mapping-out of responses may, again, decide upon the level of the lesion. For example, this will help to distinguish between a paralysis of the circumflex nerve and one of the fifth root.

I entirely disagree, also, with the pure physiologist when he dogmatizes with regard to the usefulness of electrical stimuli being confined to the faradic coil. One has proved repeatedly the truth of Lewis Jones's contention that *any* deviation from the completely developed reaction of degeneration is important and that a sluggish response to direct current stimulus is diagnostic of a lower motor lesion even in the presence of excitability by faradism, just as a brisk response to direct current stimulus, occurring concomitantly with absence of faradic excitability, indicates the existence of functioning lower motor neurones.

No investigation of a lower motor lesion, then, is complete without an accurate account of (1) skin and other sensibility, (2) voluntary muscular control, and (3) electrical responses of all relevant muscles by all the means that are clinically practicable. It is obvious that a comparison of the results of repeated observations is likely to afford valuable evidence with regard to progress.

Mr. F. H. Bentley said that the result of experiments in nerve-anastomosis in animals was to emphasize the obstructive effects (on the passage of nerve-fibres) of the intraneural scar that formed in a nerve-suture line. This scar-formation was greatly increased by any slight inaccuracy of approximation or by invasion of the nerve by the sutures at operation, with corresponding reduction in the number of fibres reaching the distal segment of nerve. In order to permit the maximum number of fibres to reach the distal end of the nerve the intraneural scar must be reduced to a minimum, and therefore extreme accuracy of approximation was an essential condition in a nerve-suture operation. In histological sections of the experiments performed it was apparent that fine silk sutures produced very little connective tissue reaction.

In experiments in grafting the limb nerves in the cat, carried out by Dr. Hill and himself, it had been shown repeatedly that an autogenous graft 3 cm. long, and of equal calibre with the recipient nerve, would bridge successfully a corresponding nerve-gap. The results reported in man were not so satisfactory, and the only nerve-grafting to be conducted with success was that of the facial nerve, after the manner of Ballance-Duel. The reason for this success lay partly in the accuracy of approximation of the ends of graft and nerve, facilitated by the bony bed in which they lay, but was due largely to the use of a graft of approximately the same calibre as the facial nerve.

The problem in grafting limb nerves was to obtain a graft of suitable size in order to secure an accurate approximation. As there was, obviously, no nerve available, this graft could only be obtained by using multiple strands of cutaneous nerve, and the experiments in nerve anastomosis suggested that the necessary degree of accuracy in approximation could not be obtained in this way, and that a completely obstructive scar would result.

The only logical possibility therefore was to use a graft of appropriate size taken from another individual, i.e. from a cadaver. In the cat such homeografts 3 cm. long were successful in bridging a nerve-gap, though not as readily successful as the autogenous grafts, since the homeografts were subject to considerable connective-tissue invasion by the host tissues. In the absence of direct experimental findings it was therefore doubtful whether regeneration would take place through long homeografts such as would be required in man.

Section for the Study of Disease in Children

President—C. PAGET LAPAGE, M.D.

[February 26, 1937]

Megaduodenum (Specimen).—T. PEARSE WILLIAMS, M.D.

R. T., male, aged 10 months at death.

History.—Birth-weight 6 lb. At the end of the first week of life projectile vomiting occurred, lasting for a few days. This type of vomiting reappeared at intervals of a few days until the infant was three months old. Each attack lasted from two to five days and was followed by intervals of slightly greater length. Breast feeding was tried for the first month and after this various artificial foods. The next five months were difficult, but slow progress was maintained and the attacks of vomiting recurred only at infrequent intervals and were not severe. More rapid progress was made during the next two months, and semi-solid food was given from the ninth month.

On 8.1.37, after having been perfectly well the previous day, the infant refused his 6 a.m. bottle, appeared to be in pain, and vomited copiously—the vomit containing prune pulp which had been ingested eighteen hours previously. Further projectile vomits followed, some being bile-stained. Water only was given, followed by small feeds of a dilute dried milk mixture. When seen on 10.1.37 at 6 p.m. dehydration was only slight and the nutrition was noted as being very good. The stomach was easily visible, distended and dilated with visible peristalsis when a little water was swallowed. The mass of the stomach extended well over to the right of the mid-line and no tumour could be felt. Sedatives, atropine, and daily lavage were advised. Improvement followed for the next forty-two hours; sudden collapse then occurred and, despite all restorative measures, death rapidly ensued.

Post-mortem report.—The length of the stomach was 9.0 cm. and of the greater curvature of the duodenum, 12.0 cm. The width of the distended duodenum was 2.5 cm. The wall of the stomach was hypertrophied, the rugæ were well marked and thickened. A considerable amount of bile-stained mucus was present and there was little or no evidence of gastritis. Mucus, heavily stained with bile, was present in the distended duodenum and the jejunum. The duodenal wall was grossly hypertrophied. The liver was normal and the gall-bladder empty and contracted. The whole of the small intestine was massed together in the mid-line and the mesentery shortened. There was no hepatic flexure of the colon and the cæcum occupied an almost central position with a short ascending colon passing across the duodenal-jejunal junction

to become a short transverse colon. There was no evidence of any inflammatory process, the abnormal position of the alimentary tract being probably a congenital defect.

I am indebted to Dr. H. W. Perkins for the post-mortem description and for the preservation of the specimen.

Dr. PARKES WEBER wondered whether it was possible to obtain a radiogram of the stomach and duodenum in such infants, as the picture of a large distended duodenum would suggest organic obstruction by a mesenteric (arterio-mesenteric) band in the last part of the duodenum, and the necessity for surgical interference.

Actinomycosis of the Lung.—SETON CAMPBELL, M.B., and A. J. HARDY, L.R.C.P., M.R.C.S. (for Dr. DONALD PATERSON).

D. W., female, aged 9 years. First shown at the meeting held in June 1936.

History.—Perfectly well up to May 1935, when she became increasingly listless and began to lose weight. During the first week of June, her mother noticed a small, slightly tender, firm lump developing on the right side, a few inches below and lateral to the nipple. There was also a short dry cough, and on June 10, 1935,



FIG. 1.—Showing extensive subcutaneous sinuses.

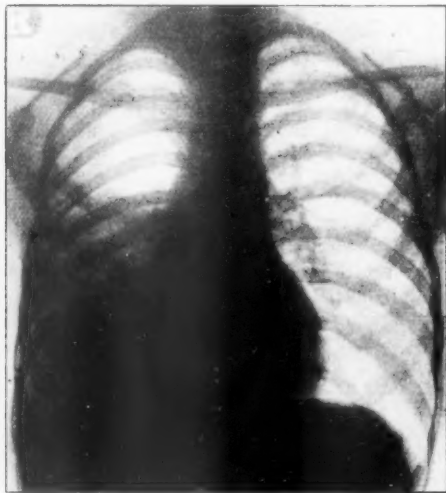


FIG. 2.—Showing right basal fibrosis, thickened pleura, and displacement of the mediastinum to the right.

she was seized by a sharp pain on the right side and became somewhat breathless. The swelling on the right side was opened, and the pus obtained showed the typical Gram-positive branching mycelia of actinomycosis. Treatment at that time was: (1) Large doses of potassium iodide by mouth; (2) Local X-ray treatment (Dr. Allchin).

Since April 1936, the child has been at a convalescent home. She returned to hospital on February 3, 1937.

On examination.—She appears perfectly happy and well. Colour good, temperature 98° - 100° F.; pulse 120; respirations 32. No alteration in weight during the last year. Numerous sinuses over right posterior lower thorax and also over lumbar region (fig. 1); very slight discharge from these. Physical signs of fibrosis present in right lower thorax, together with signs of enlarged heart.

Laboratory findings.—Smear from discharging sinus: No evidence of Gram-positive branching mycelia. Blood-count: W.B.C. 17,000 per c.mm. Sedimentation rate: 5 mm. at the end of one hour. Wassermann reaction negative. Mantoux test (1:100) negative.

Radiological examination.—Thickened pleura and fibrosis of right lower lobe. Heart and mediastinum displaced to right (fig. 2).

Treatment.—(1) Gradually increasing injections of mixed actinomycosis vaccine; (2) X-rays to the affected parts.

Dr. K. H. TALLERMAN said he felt that the prognosis in this disease was so bad that the outcome in this case would be fatal. He recalled a similar case in a child under the care of Dr. Maitland-Jones in the Children's Department of the London Hospital, who had previously been shown before the Section, and who had actually lived for about three and a half years after contracting the disease before succumbing; this child had been treated with massive doses of iodide only, and for a period the improvement had been remarkable.

Influenzal Meningitis with Complete Recovery.—T. PEARSE WILLIAMS, M.D.

J. N., female, aged 9 months.

History.—On 22.8.36 she fell out of her cot and struck her head. She remained drowsy after the fall and was irritable if disturbed.

24.8.36: Vomited, refused food, went blue, and was admitted to hospital.

On admission.—Pale, collapsed, blue lips, anterior fontanelle bulging, hæmatoma over right parietal region. No paresis, no rigidity. Reflexes present, pupils reacted. Temperature 102.0° . Pulse 132. Respirations 64.

Progress.—Fever persisted, rising to 103.8° on 27.8.36, when vomiting began again after feeds. Four days later the infant was drowsy in the morning and had a series of convulsions during the afternoon. During the spasm the head was turned to the right and the left arm twitched. A 20% solution of magnesium sulphate was given per rectum. The convulsions ceased but the child remained unconscious with occasional twitching of the limbs. Fever, up to 104° , persisted.

1.9.36: Examined by the exhibitor. Rigidity of neck muscles noted, with well-marked bilateral Kernig's sign. Fontanelle bulging. Infant very drowsy.

Lumbar puncture was performed, the fluid being under pressure, depositing pus and giving a free growth of influenza bacilli. Daily lumbar puncture was carried out, with a free drainage, up to 11.9.36. The only complicating features of this period were vomiting and a reluctance to take food.

14.9.36: The infant appeared to be doing well and was much brighter, but on the following day she became drowsy again and showed head retraction. A further lumbar puncture was made and 25 c.c. of fluid withdrawn. Notable relief was obtained from this drainage and it was repeated again on 17.9.36 and 19.9.36. The temperature had fallen on September 16 to 99.0° and became normal and steady from 28.9.36. Examination of C.S.F. (11.9.36) showed a very few bacilli only and very little pus. The last tapplings gave only a clear fluid.

20.10.36: Infant seen at out-patient department. She had been quite well, had continued to gain weight and showed no abnormal signs.

Dr. DONALD PATERSON said he presumed that Dr. Pearse Williams referred to Pfeiffer's bacillus when he spoke of influenzal meningitis. At a meeting of the Section he (Dr. Paterson) had shown a case of recovery from this infection after about seventy lumbar punctures. The child, however, was left with a mild hydrocephalus.

Dr. Silverthorne, of Toronto, in conversation, had told him that the Connaught Laboratories of Toronto now had a serum for this disease, and that he had had twelve cases of complete recovery, which he proposed reporting in due course.

Cirrhosis with Jaundice: Cholecystgastrostomy.—P. R. EVANS, M.B.
(for WILFRID SHELTON, M.D., and HAROLD EDWARDS, M.S.).

Girl, aged 9 years, complaining of jaundice.

Family history.—Parents healthy; patient is eldest child. Mother has had one tubal pregnancy and one healthy daughter. No miscarriages.

* *Previous health.*—Good. Measles, mumps, and whooping-cough.

History of present illness.—April 1935, onset of jaundice, followed by diarrhoea and vomiting. Jaundice has continued since, with exacerbations, but the vomiting and epigastric pain have become progressively rarer. Child seems feverish at times. Stools pale and bulky. Urine high coloured.

On examination (December 1935): Scleral and cutaneous jaundice; spleen three fingerbreadths, liver three fingerbreadths, below costal margin. Urine: albumin, bile salts and pigments present.

Jaundice almost disappeared in one month and urine became clear; spleen one fingerbreadth, liver two fingerbreadths, below costal margin, while hexamine was being given. Styes and small boils appeared.

6.12.35: R.B.C. 4,140,000; Hb. 94%; C.I. 1.14; retic. 1.2%; W.B.C. 10,000 (polys. 50%; lymphos. 46%; eosinos. 2.5%; monos. 1.5%). No increase in blood fragility. Van den Bergh reaction: Hæmobilirubin 1.2 mgm. per 100 c.c.; cholebilirubin 0.8 mgm. per 100 c.c. Wassermann reaction: 11.12.35, weak positive; 24.12.35, positive. (Mother's Wassermann reaction: weak positive.) Treated with bismostab injections. Between January and March 1936 ten injections (total 5 c.c. were given). Skiagram of right knee, February 1937 (see figure, p. 39): The transverse striations in the metaphysis may represent increased calcification due to the bismuth treatment (see Caffey, J., *Am. J. Dis. Child.*, 1937, 53, 56).

March 1936: Readmitted to hospital because of increase of jaundice and epigastric pain.

10.3.36: R.B.C. 4,100,000; Hb. 82%; C.I. 1.0; retic. 1%; W.B.C. 6,600 (polys. 70%; lymphos. 28%; eosinos. 1%; monos. 1%). Hæmobilirubin 1.25 mgm. per 100 c.c.; cholebilirubin 3.35 mgm. per 100 c.c.

Lævulose tolerance test:

Hours after 50 grm. lævulose	0	$\frac{1}{2}$	1	1 $\frac{1}{2}$	2
Blood-sugar %	0.066	0.088	0.109	0.117	0.131
Urine: Sugar + +		Acetone 0			

Cholecystogram.—Gall-bladder outlines shown faintly, at twenty hours.

3.6.36: Cholecystgastrostomy performed. Gall-bladder rather large, white and thick-walled. Common bile-duet looked normal. Liver surface grossly nodular. Piece of liver removed for biopsy showed multilobular cirrhosis with lymphocytic and plasma-cell infiltration and new formation of bile-duets.

Apart from massive collapse of the right lung, recovery was uneventful, but no effect on the jaundice has been noticed.

Present condition.—Has not returned to school. Jaundice always present, but varies in intensity; urine dark (bile pigments present, salts absent); stools vary in colour. Some epigastric pain; much flatulence. Liver hard, little enlarged; spleen 2 fingerbreadths below costal margin.

17.2.37: R.B.C. 3,940,000; Hb. 77%; C.I. 0.98; W.B.C. 3,800 (polys. 47%; lymphos. 47%; eosinos. 4%; monos. 2%).

Gastric residuum contains free hydrochloric acid, much bile. Wassermann reaction doubtful.



Right knee, February, 1937.

Comment.—The Wassermann reaction is known to be unreliable in the presence of jaundice (Lange, 1922), but the mother had a weak positive reaction: there was no clinical evidence to suggest a diagnosis of syphilis, and the clinical and pathological picture is unlike late congenital syphilitic hepatitis. Rolleston and McNee (1929) suggest that after recovery from congenital syphilis the liver may be unusually susceptible to agents which cause multilobular cirrhosis, but the presence of jaundice and absence of ascites and collateral venous circulation remove the case from the class of portal cirrhosis.

It was hoped that laparotomy would reveal low biliary obstruction as in the cases of Strauss and others (1933), but no such obstruction was found. Clinically

the symptoms are those of Hanot's syndrome (1876), except for the presence of bile in the urine and the pallor of the stools, but a diagnosis of subacute hepatic atrophy following catarrhal jaundice is the most credible.

REFERENCES

- HANOT, V. (1876), "Étude sur une forme de cirrhose hypertrophique du foie", Paris.
LANGE, C. (1922), *Klin. Wchnschr.*, **1**, 1040.
ROLLESTON, H., and MCNEE, J. W. (1929), "Diseases of the liver", London, p. 415.
STRAUSS, A. A., STRAUSS, S. F., CRAWFORD, R. A., and STRAUSS, H. A. (1933), *J.A.M.A.*, **101**, 1065.

Discussion.—Dr. WILFRID SHELDON said that he did not regard syphilis as the cause of the present state of the liver, because of the prolonged jaundice, which had continued in spite of the Wassermann reaction becoming negative under antisyphilitic treatment. The gall-bladder was drained, in the hope that this might relieve the jaundice; he had known relief follow in the case of another child who had been operated upon in similar circumstances. The present patient, however, had not benefited by the operation.

Dr. PARKES WEBER said he believed that multilobular cirrhosis of the liver might occur in children who as infants had been affected by congenital syphilitic hepatitis of the well-known intercellular and unilobular type. He believed also that every hepatic cirrhosis, if the process progressed, became multilobular (or partially multilobular), even if it had been unilobular at the commencement. The idea of the existence of a cirrhosis of long duration, which was strictly unilobular by microscopical examination, was a myth.

Dr. JEWESBURY said that he had shown a similar case fairly recently at a meeting of this Section (see *Proceedings*, 1936, **29**, 737 (Sect. Dis. in Child., 25)).

Undulant Fever.—C. HARDWICK M.B. (for Dr. DONALD PATERSON).

B. G., male, aged 5 years, was admitted to Great Ormond Street Hospital on February 5, 1937, with a history of the sudden onset of pyrexia at the beginning of January; the fever lasted fourteen days. The temperature was normal every morning but rose in the evenings to 102° F. The child appeared to be quite well, but towards evening was noticeably tired and flushed.

Appetite good; bowels acted regularly; no sickness, undue sweating, or complaint of pain.

On examination.—A healthy, well-covered child. No abnormal physical signs in chest. Cardiovascular system normal. Tonsils small; no glandular enlargement. Spleen enlarged to about two fingerbreadths below left costal margin. Temperature normal while in hospital.

*Sedimentation rate (micro-method) 9 mm. in first hour. Mantoux and Wassermann reactions negative. Agglutination with *B. abortus* was positive up to a titre of 1:1,000; there was slight agglutination with *B. melitensis*.

Dr. JEWESBURY said that he had recently seen a girl aged 6 years who had been running an irregular temperature without anything to account for it for about three weeks. The case proved to be one of undulant fever. The blood showed a leucopenia with lymphocytosis, the serum agglutinated against *Brucella abortus* to a dilution of 1:500, and the bacillus was isolated from the blood on culture. The child lived under the best conditions, and the milk used was pasteurized milk supplied by one of the big London dairy combines. Another child in the family was unaffected. The case raised the question as to whether pasteurized milk (if properly pasteurized) is "safe" milk from the point of view of this type of infection.

Exomphalos associated with Volvulus Neonatorum : Result six and a half years after Operation.—HAROLD EDWARDS, M.S.

V. S., a girl, aged 6 years 10 months.

Born at 9 a.m. on May 27, 1930, and admitted two hours later to the Evelina Hospital. The cord had been tied off some distance away from the abdomen and the intervening portion was broadened and fused at a wide base with the abdominal wall. Its wall was a thin transparent membrane through which coils of intestine were plainly visible. These were blue in colour and obviously congested. It was thought that a volvulus neonatorum co-existed with the exomphalos.

Operation under open ether anaesthesia (Dr. Wright).—The membrane was cut away at its junction with the abdominal wall. It was then noted that the caecum lay on the left side, and that the whole of the mid-gut was rotated around a narrow pedicle. A thin sheet of membrane ran from the mesentery to the fundus of the sac (? anterior mesentery). The volvulus was readily untwisted. With great difficulty the intestines were placed inside the abdominal cavity and considerable force had to be used. There was no possibility of suturing the abdominal layers separately, and the wound was therefore closed with four tension stitches of silkworm gut passing through all coats and tied very tightly.

The operation was followed by a mild chest complication which rapidly subsided, and, despite considerable difficulty in feeding during the next two months, the infant made a good recovery.

Dr. P. R. EVANS described a case in which there had not been a volvulus and no operation had been performed. The infant was admitted to hospital the day after he was born, and was seen to have a transparent sac about 10 cm. in diameter, containing liver and intestine, the umbilical stump being attached to the lower part. There was an indirect



Dr. Evans' case of exomphalos with bilateral inguinal hernia. Aged 8 weeks.

inguinal hernia on each side. Dressings of acriflavine and paraffin, and later paraffin alone, were applied, and the sac became opaque and smaller in size. Skin grew over it from the sides. The illustration shows the condition in the eighth week, with epithelium over the upper and outer parts and clean granulation tissue in the centre.

There was no constipation but vomiting was frequent. From the seventh week onward weight was gained satisfactorily. Unfortunately a ward infection with whooping-cough proved fatal in the fourteenth week. Autopsy showed the appendix and the cæcum, with long mesenteries, in the right upper quadrant of the abdomen. The ductus arteriosus was patent.

Cleido-cranial Dysostosis.—REGINALD C. JEWESBURY, D.M.

E. T., male, aged 6 years.

Only child. No other relative affected. Labour normal. Breast-fed for 9 months. Birth-weight $7\frac{1}{2}$ lb. Weight at 1 year, 17 lb.; at 6 years, 32 lb.

Clavicles: Only sternal ends (about $\frac{1}{2}$ in.) palpable (fig. 2).



FIG. 1.—Cleido-cranial dysostosis.

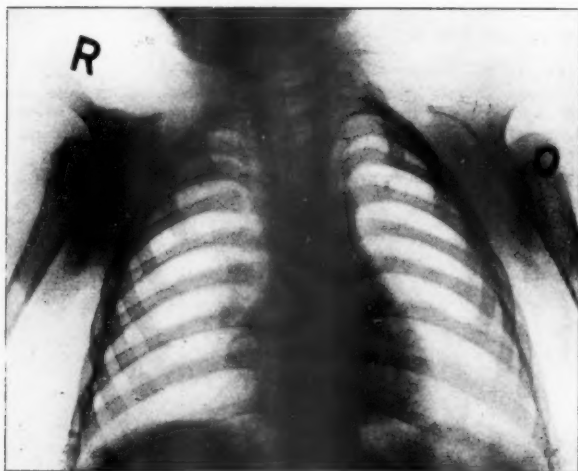


FIG. 2.—Thorax showing complete absence of both clavicles.

Skull: Large anterior fontanelle. Depression over posterior fontanelle (figs. 3 and 4).

Dr. PARKES WEBER said he wondered whether isolated cases of the condition were known to exist, that is to say, cases in which accurate and complete family history had been obtained, with an entirely negative result.

alone,
n the
r the

ward
ough
with
was

for

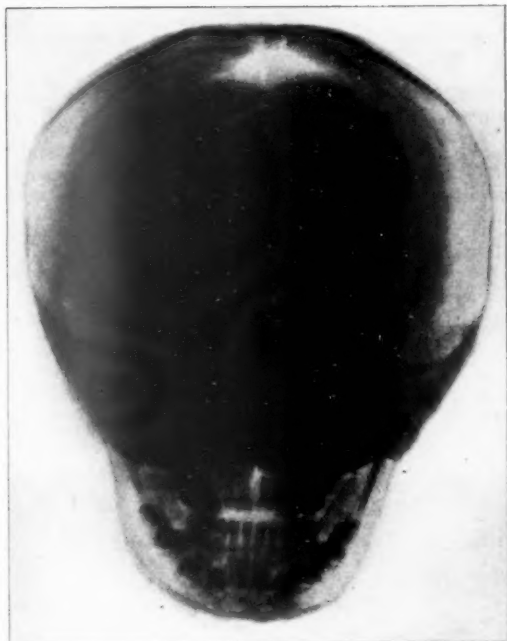


FIG. 3.



FIG. 4.

FIGS. 3 and 4.—(Dr. Jewesbury's case of cleido-cranial dysostosis) Showing late closure of anterior fontanelle and narrowing of base of skull.

MAY—DIS. IN CHILD. 2 *

Complete Transposition of Viscera.¹—G. H. NEWNS, M.D. (by courtesy of DONALD PATERSON, M.D.).

B. B., a boy, aged 6 years and 1 month, had whooping-cough and measles in 1935; since then has had a persistent cough. Has always been subject to attacks of bronchitis. Admitted for investigation to the Hospital for Sick Children in November 1936.

Family history.—The only other child, a boy aged 8, is normal. No consanguinity between the parents. Mother's brother is said to have dextrocardia.

Condition on admission.—Well nourished. No cyanosis; no finger-clubbing. Visible pulsation to right of sternum; apex-beat localized in fourth right intercostal space. Harsh systolic murmur audible over whole precordium but loudest at base to right of sternum over pulmonary area. Pulmonary second sound audible. Adventitious sounds in both lungs but no sign of consolidation. Large firm swelling

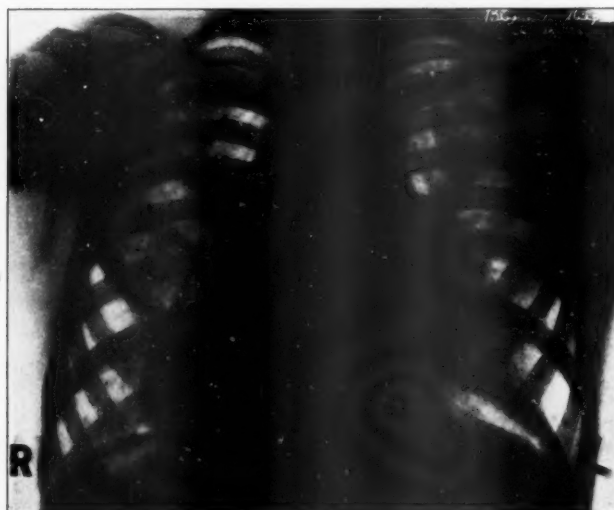


FIG. 1.—The chest: showing dextrocardia.

in epigastrium; moved with respiration and varied much from day to day; appeared to be distended stomach. The right testicle is undescended.

Investigations.—Chest: dextrocardia; some mottling in lungs (fig. 1). Barium meal shows stomach on right (fig. 2). Mantoux reaction negative. Sedimentation rate: 7 mm.

Blood-count: R.B.C. 4,420,000; Hb. 68%; W.B.C. 6,450 (polys. 60%; lymphos. 36%). Electrocardiogram: Not typical of dextrocardia; inversion of T₁, T₂, P₂, and P₃. Left axis deviation.

¹ This case was shown at the meeting held on November 27, 1936, but its publication was postponed in order that an illustration might be obtained.

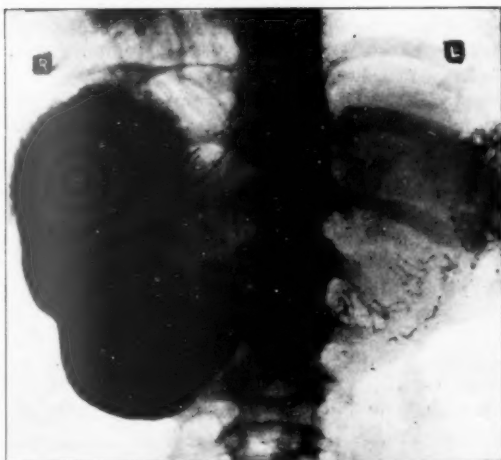


FIG. 2.—Barium meal. The stomach is shown on the right.

Discussion.—Dr. BERNARD SCHLESINGER said that the electrocardiogram which he had taken in this case was not the usual one found in transposition of the heart, in that the P wave was not inverted in Lead I in company with the T wave. Otherwise the changes conformed to those generally found in this condition. No doubt the presence of a congenital lesion within the heart, in addition to the transposition, accounted for the electrocardiographic anomaly mentioned.

Dr. PHILIP ELLMAN said that at a meeting of the Clinical Section in 1935 he had shown a case of dextrocardia with complete transposition of viscera.¹ In addition to the dextrocardia, the patient had congenital pulmonary stenosis and pulmonary tuberculosis. The electrocardiogram was typical of those seen in dextrocardia with complete *situs inversus*. On investigation of the family tree the parents were found not to be first cousins, and there was no evidence of any abnormality in other members of the family.

Specimen from a Case of Staphylococcal Pneumonia.—H. J. WALLACE, M.R.C.S., L.R.C.P. (introduced by Dr. K. H. TALLERMAN).

P. S., female, aged 4 weeks.

History.—The infant had appeared ill for two days. There was no cough or vomiting and the bowels were regular. On 1.12.36 she collapsed and was admitted to hospital.

Past history.—Full-term child. Normal delivery. Birth-weight 6½ lb. Breast-fed for two weeks, then bottle-fed on Grade A milk and water, and later on sweetened Nestlé's milk mixture.

Family history.—One other child, healthy. Parents healthy. No history of illness in the home.

On admission.—Temperature 103·5°. Respirations 30. Pulse 140. Weight 6 lb. Very ill, cyanosed, and respirations feeble. Examination of the chest showed crepitations at both bases, especially marked at the left base. No other physical signs.

¹ *Proceedings*, 1935, 28, 303 (Clin. Sect., 11).

While in hospital the child's condition became rapidly worse, respiration proceeded in a series of six or seven gasps with a period of apnoea up to one minute between each respiratory effort. Death occurred thirty hours after admission.

Post-mortem (performed twelve hours after death by Dr. David Haler).—No rigor mortis. Multiple petechiæ. Umbilicus and umbilical veins normal. Excess of free fluid in the abdominal cavity. Respiratory system: Larynx and trachea showed mucopus. The left pleural cavity showed a large inspissated empyema covering the whole of the lungs. The lower lobe of the left lung was replaced by multiple abscesses, some being subpleural. At the left apex there was a large subpleural bulla. The right lung showed bronchitis and compensatory emphysema. Heart: Muscle flabby. Nodules of uncertain nature on mitral valve. Suprarenals: Enlarged, especially the left which contained two adenomata. Alimentary system: Nothing abnormal. Liver: Flabby.

Owing to limited parental permission, no examination was possible of skull, brain, and ears.

Bacteriology.—(1) From empyema: In direct film, pus cells and Gram-positive cocci. No influenza bacilli. Culture on blood-agar and Fildes' agar showed *Staphylococcus aureus*, but no influenza bacteria. (2) From the lung abscess: Similar result.

Section of Comparative Medicine

President—GEORGE W. DUNKIN, M.R.C.V.S.

[February 24, 1937]

The Lesions Produced in the Organs of the Rabbit by Single and Repeated Intravenous Injections of BCG: A Preliminary Note

By J. R. M. INNES

(*Institute of Animal Pathology, Cambridge University*)

THE aim of these experiments was to throw light on the development of immunity in calves vaccinated with BCG by the intravenous route. Buxton and Griffith (1933), and Buxton, Griffith, and Glover (1935), showed that calves resisted an intravenous injection of virulent tubercle bacilli better after an intravenous injection of BCG than after an intratracheal or subcutaneous one.

The intravenous route was therefore used in later experiments, and it was observed that BCG was rapidly eliminated from the body. For example, three calves died or were killed nine, fourteen, and twenty-five days respectively, after the injection of BCG; cultures were prepared from the lungs, and colonies were most numerous in the first animal and least in the last. In another experiment, five calves were inoculated intravenously with 100 mg. BCG; one calf was killed seventy-one days later and no acid-fast bacilli were found microscopically. Cultures were also prepared from various sites but only one colony of BCG was obtained from the left bronchial lymph-gland. From a second calf, killed at the hundred and twentieth day, no cultures of acid-fast bacilli were obtained. These results seemed to imply that, so far as cultural experiments were concerned, BCG disappeared from the tissues before the fourth month. The remaining three calves continued to react to tuberculin for several months although with decreasing intensity. Two were completely resistant to oral administration of virulent tubercle bacilli seven to ten months after vaccination, while the third, although it became infected after thirteen months, possessed a greater degree of resistance than unprotected controls.

In addition to the persistence of immunity after a primary injection, attention was directed to the effects of reinforcing doses of BCG. A second dose of 100 mg. BCG, given to calves at six, nine, and twelve months respectively, after the initial injection, definitely reinforced the immunity. Often, however, the second injection induced a severe reaction, which in two instances was followed by the death of the calf. It seemed, therefore, that if the pulmonary tissue was in this high state of sensitivity, a large proportion of the vaccinating dose might be rejected. It has not been possible to test this point in calves but the rabbit experiments described below, in which reinoculation was carried out at various intervals, suggest that this does occur.

The main object of this investigation, therefore, was to study the genesis and fate of the lesions produced in rabbits by single and repeated doses of BCG, with the hope that the results might throw some light on the immunity developed in the calf after vaccination with BCG. It was also hoped that additional information

might be obtained about the formation of the tubercle. Huebschmann (1928), Cunningham and Tomkins (1928 and 1931), Sabin, Doan, and Forkner (1930), believe that the entire development of the tubercle is an exudative process, all the cellular constituents being derived from the blood and that the lipoids of the tubercle bacillus contain a maturation factor for the monocytes and epithelioid cells. Krause (1927) contends that it is essentially a proliferative process, and states that although leucocytes, red blood cells, &c. may enter into the structure of the nodular tubercle, they are not an essential part of this lesion. Pagel (1932) has shown that some tubercles begin in exudation but later elicit a proliferative response, and that others are essentially proliferative from the beginning.

The origin of the fibrous tissue in the tubercle is also debatable. Does it grow in by proliferation of the surrounding fixed mesenchyme cells? Are the mononuclear phagocytes and their derivatives, the epithelioid cells, capable of forming it? (Maximov, 1935). Or is it a precipitation process arising from the production of a specific factor from the vascular endothelium and other mesenchyme cells? (Day, 1936).

Many workers have shown that BCG may produce tubercles. Lurie (1934) stated that BCG organisms are soon destroyed in the body after inoculation, for although the injection of 1 to 2 mg. produced typical tuberculous lesions in the lungs of rabbits, within two months the lesions and bacilli had disappeared. The destruction of the bacilli usually coincided with the development of hypersensitivity. Rosenthal (1936) made intracardiac injections of 10 to 15 mg. BCG into guinea-pigs and showed that distinct lesions could be found in the lungs after a few hours. The nodules which formed were initiated either by an accumulation of leucocytes or by a proliferation of epithelioid cells. By the end of the first week typical tubercles made their appearance. Their regression was accompanied by the entrance of lymphocytes and the lesions disappeared within one to three months. Fibrosis was rare and caseation and necrosis were absent. The histological differences of lesions after intracutaneous injection of BCG and virulent tubercle bacilli have been described by Pagel (1929).

Methods.—Ninety rabbits were injected intravenously with graded doses of BCG ranging from 0.005 to 10 mg. Most of the animals have been killed at intervals from 24 hours to 290 days, but the experiment is not yet finished. Various organs were examined histologically and attempts were made to recover the organisms from the lungs by cultural methods.

Synopsis of results.—Within twenty-four hours of the injection of 5 to 10 mg. BCG, innumerable cellular foci were discernible in the lungs. These foci, containing clumps of acid-fast bacilli, formed septal thickenings which had apparently followed the lodgment of the bacilli in the capillary walls. The cell aggregations consisted of polymorphonuclear leucocytes and phagocytes, and appeared responsible for the initial localization of the bacilli. The polymorphonuclear leucocytes took no further part in the formation of the tubercle. By proliferation of the fixed mesenchyme cells and/or by localization, and subsequent proliferation, of monocytes, these septal thickenings increased in size and by the sixth day formed considerable bulges abutting, but not exuding, into the alveolar spaces, so that at this stage the lesions were thus strictly intracapillary. By further cellular proliferation in an intramural direction the classical tubercle made its appearance between 12-21 days, when the lungs were riddled with such lesions. In the centre of the tubercles there was a conglomerate mass of epithelioid cells and at the periphery a well-marked zone of lymphocytes. Polymorphonuclear leucocytes were either scanty or absent. Necrosis was present in only a small proportion of the tubercles and Langhans's giant cells were few and not necessarily associated with necrosis. (Medlar (1926), Day (1934), and others have contended that giant-cells in a spontaneous tubercle are post-necrotic in development). The margin of the tubercle projecting into the

alveoli was composed of alveolar epithelium which, at a later stage, often showed a distinct metaplastic cubical transformation. Many of these mature tubercles, which were first seen within two or three weeks of the injection, persisted, and were present, though in comparatively small numbers, in the lungs of rabbits killed as late as 205 days after injection. Many must have regressed, therefore, at a relatively early stage. As Rich (1929) has stated, in connexion with the fate of some tubercles in the progressive disease, the cells appear simply to separate and wander off after the bacilli have died or been destroyed. Nevertheless, tubercles persist in the lungs of these rabbits long after bacilli can be recovered by culture, and the reason for this persistence is therefore at present unknown. No fibrosis was seen at any stage by ordinary stains, but by using a special silver impregnation method for reticulum, e.g. Wilder (1935), a well-marked argyrophil fibrillary network was seen enmeshing the tubercles in the lungs of rabbits killed as early as 21 days after injection. This formed a thick felt-work at the periphery of the tubercle (the fibres here anastomosing with the normal pulmonary and vascular reticulum), with numerous fibrils ramifying between the epithelioid cells and penetrating into the centre. In the later stages (e.g. in the lungs of rabbits killed 114-205 days after injection), this fibrillary basket-work was an outstanding feature of the tubercles. The subsequent fate of this process is still to be determined. As no small scar-like foci of such fibrils can be seen in the lungs in the late stages, this proliferation of argyrophil fibres may also be a reversible process. As other workers have suggested, most of these tubercles in the lungs probably resolve completely within a few months, but they may persist as long as 205 days after injection—much longer than has hitherto been suspected. In three animals which were killed 290 days after injection of 10 mg. BCG, no lesions could be determined in the lungs.

In those tubercles which had persisted, increased vacuolation of the epithelioid cells, the appearance of tissue crevices between these cells, and the entrance of blood-cells, appeared to be progressive changes. In such cases many epithelioid cells appeared to have wandered into the neighbouring alveoli.

The mechanism by which necrosis occurs in some of the tubercles is unknown. It is almost certainly not a case of tissue ischaemia caused by an avascular condition of the tubercles, as has been suggested by many workers in the case of tuberculous.

The lesions in the tracheobronchial lymph nodes never reached the same intensity as in the lungs. In the early stage the nodes were macroscopically swollen, and histologically the essential change appeared to be an intense sinus catarrh, the sinusoids being filled with solid masses of macrophages (desquamated and proliferated littoral cells). No caseation occurred, and the glands in the late stages were unchanged.

Variations in the lesions in the lungs of rabbits injected with smaller doses of BCG than 5 mg. were purely quantitative. For example, no lesions could be seen in the organs of rabbits killed 20, 34 and 44 days after the injection of 0.005 mg. BCG.

The reinoculated rabbits varied considerably in their response to the second dose. Most of the rabbits reinjected as early as 21 days, and as late as 114 days, after the initial injections were not severely affected but a small number died. Some showed acute respiratory distress and died within 24 hours, but in others there was a latent period of about 7 days before this reaction. The lungs in all these animals were voluminous, dark reddish-grey in colour, and consolidated throughout. Histologically, the outstanding feature was the intense exudation into the alveoli of red blood corpuscles and cells indistinguishable from the epithelioid cells. The same type of pneumonic lesion has been observed in the lungs of calves which died under similar circumstances. In the lungs of those animals which survived the reinoculation and were killed at varying intervals, the reaction was similar in type to that which followed the initial dose.

Acid-fast bacilli could be demonstrated in the tubercles in sections of the lungs as late as 114 days after injection, but most of these must have been dead, as the organism could not be recovered by cultural methods after 62 days.

The experiments suggest that in the case of calves there is a considerable degree of resistance long after the "vaccinating" organism has disappeared, unless it is postulated that a few "vaccinating" bacilli persist but are not recoverable by culture. While the mechanism of this immunity is at present unknown, it might be tentatively suggested that the protection is associated with a tissue reaction like that discernible in the lungs of rabbits many months after the intravenous injection. In revaccination experiments in calves, it is possible that the BCG organisms are very rapidly eliminated from the body, and that the immunity results from the marked cellular response which they evoke.

Thanks are due to my colleague, Mr. R. E. Glover, for his help and criticism, and for his assistance in undertaking the bacteriological work necessary for these experiments.

REFERENCES

- BUXTON, J. B., and GRIFFITH, A. S. (1931), *Lancet* (i), 393.
BUXTON, J. B., GRIFFITH, A. S., and GLOVER, R. E. (1935), Fourth Report, Inst. Animal Path., Cambridge Univ.
CUNNINGHAM, R. S., and TOMKINS, E. H. (1928), *Am. Rev. Tuberc.*, **17**, 204; (1931), *ibid.*, **23**, 71.
DAY, T. D. (1934), *J. Path. and Bact.*, **38**, 175; (1936), *ibid.*, **43**, 49.
HUEBSCHMANN, P. (1928), *Path. Anat. der Tuberkulose*, Springer, Berlin.
KRAUSE, A. K. (1927), *Am. Rev. Tuberc.*, **15**, 137.
LURIE, M. (1934), *J. Exper. Med.*, **60**, 163.
MAXIMOV, A. A., and BLOOM, W. (1935), "Textbook of Histology", Saunders, Philadelphia and London.
MEDLAR, E. (1926), *Am. J. Path.*, **2**, 291.
PAGEL, W. (1929), *Klin. Wchnschr.*, **8**, 170.
Id. (1932), *Beitr. z. Klin. d. Tuberk.*, **79**, 383.
ROSENTHAL, S. R. (1936), *Arch. Path.*, **22**, 348.
RICH, E. A. (1929), *Bull. Johns Hopkins Hosp.*, **44**, 273.
SABIN, DOAN, and FORKNER (1930), *J. Exper. Med.*, **52**, Suppl. 3.
WILDER, H. C. (1935), *Am. J. Path.*, **11**, 517.

Section of Odontology

President—W. WARWICK JAMES, O.B.E., F.R.C.S., L.D.S.E.

[January 25, 1937]

Vinyl Ether for Dental Anæsthesia

By VICTOR GOLDMAN, L.R.C.P., M.R.C.S., D.A.

ABSTRACT.—*Properties:* Vinyl ether, $\text{CH}_2:\text{CH}_2:\text{O}:\text{CH}_2:\text{CH}_3$, a volatile liquid. Lipoid-soluble but highly inflammable.

Toxicity.—Has little effect on liver function; overdoses produce respiratory paralysis, but not cardiac paralysis.

Indications.—Replaces ethyl chloride for short operations, and can be added to gas and oxygen instead of ether or chloroform. Is a safe and portable anæsthetic for the general practitioner.

Administration.—Open method convenient, but not very satisfactory, a closed method produces better anæsthesia. Special inhaler described and illustrated.

Vinyl ether is obtainable in ampoules of 3 c.c., a sufficient quantity for the average case.

Induction is rapid; signs of anæsthesia described. Patient's colour remains excellent.

Apparatus required when vinyl ether is to be added to gas-and-oxygen.

RÉSUMÉ.—*Propriétés:* l'éther vinyl, $\text{CH}_2:\text{CH}_2:\text{O}:\text{CH}_2:\text{CH}_3$, liquide volatil, soluble dans les lipoides mais très inflammable.

Toxicité: Effet peu considérable sur la fonction du foie. Les doses trop fortes causent une paralysie respiratoire mais pas de paralysie cardiaque.

Indications: Remplace le chlorure d'éthyle pour les opérations de courte durée, et peut être associé à l'anesthésie au protoxyde d'azote-oxygène, à la place de l'éther ou du chloroforme. Anesthésique sans danger et facile à transporter pour le praticien.

Administration: La méthode ouverte est commode, mais peu satisfaisante; une méthode fermée produit de meilleurs résultats. Un appareil spécial est décrit et illustré.

L'éther vinyl s'obtient en ampoules de 3 c.c., quantité suffisante pour un cas ordinaire.

L'induction est rapide. Description des signes d'anesthésie. Le teint reste toujours excellent.

Description de l'appareil nécessaire pour l'administration combinée avec le protoxyde d'azote.

ZUSAMMENFASSUNG.—*Eigenschaften:* Vinyläther, $\text{CH}_2:\text{CH}_2:\text{O}:\text{CH}_2:\text{CH}_3$, flüchtige flüssigkeit; lipoidlöslich; entzündlich.

Giftigkeit: Keine nennenswerte Wirkung auf die Leberfunktion. Überdosierung erzeugt Atemlähmung aber keine Herzlähmung.

Indikationen: Ersetzt Chloräthyl für kurze Operationen, und kann an Stelle von Äther oder Chloroform zu Gas-Sauerstoff zugesetzt werden.

Darreichung: Die offene Methode ist bequem aber nicht sehr befriedigend, eine geschlossene Methode gibt bessere Narkose. Ein besonderer Inhalationsapparat wird beschrieben und abgebildet.

Vinyläther ist in Ampoulen von 3 c.c. erhältlich. Diese Menge genügt für einen gewöhnlichen Fall.

Die Induktion geht sehr rasch vor sich. Beschreibung der Narkoseerscheinungen. Die Gesichtsfarbe bleibt ausgezeichnet.

Beschreibung der notwendigen Apparatur in Fällen in denen Vinyläther als Zusatz zu Lachgas-Sauerstoff gebraucht werden soll.

MAY—ODONT. 1

My chief communication this evening is a short film, demonstrating a method of anaesthesia for short dental operations which has been employed successfully in 850 cases during the past ten months at the Eastman Dental Clinic.

Properties.—Vinyl ether, di-vinyl oxide, has a formula of $\text{CH}_2 : \text{CH}_2 : \text{O} : \text{CH}_2 : \text{CH}_2$. It is a very volatile liquid, and is highly inflammable. It has a peculiar odour, said to be garlic-like in character. It acts as an anaesthetic on account of its solubility in lipid substances. The anaesthetic properties deteriorate rapidly on exposure to light and air. In ampoules vinyl ether seems to keep indefinitely.

Toxicity.—Experiments have shown that it is the least toxic of the lipid soluble anaesthetic agents at present in use. Bourne and Raginsky (1935) by means of injecting bromsulphalein, a dye excreted by the liver, demonstrated that there was no retention of the dye during vinyl ether anaesthesia, though retention was marked following chloroform anaesthesia. Moliter (1936) has confirmed these findings in a novel but direct manner. He tied a canula into the common bile-duct of a rabbit, and by both counting the drops of bile as excreted, and measuring the total quantity collected in a given time, he was able to make exact estimations of liver function during anaesthesia. These experiments showed that during the administration of vinyl ether there was no change from normal in the rate of excretion of bile, but during chloroform anaesthesia excretion almost ceased. In one interesting experiment a rabbit was anaesthetized by means of a mixture of 95% nitrous oxide and 5% oxygen; this caused bile excretion to cease almost entirely. After a time the percentage of nitrous oxide was reduced to 80, the oxygen being increased proportionately to 20%, and sufficient vinyl ether was added to maintain deep anaesthesia; immediately the excretion of bile was recommenced. Here, in fact, we have the strongest condemnation of sub-oxygenation that has been produced experimentally.

We have seen that vinyl ether does not cause liver damage, but overdosage does produce respiratory paralysis, and here again Hans Moliter has comforted us with a series of animal experiments which show that this new anaesthetic has a remarkable factor of safety. Rats were placed in an atmosphere of vinyl ether until respiration ceased, and so long as they were removed in under fifteen seconds, spontaneous recovery occurred in every case. Apparently cardiac failure only occurs as a secondary manifestation of respiratory paralysis.

Indications.—Vinyl ether in dental practice can replace both ethyl chloride and "straight gas". Patients, especially children, recover more rapidly than after ethyl chloride and seem to feel better than after plain nitrous oxide; this I believe to be owing to the absence of oxygen deprivation. It does not replace nasal gas-and-oxygen given by an expert, but it is a useful adjuvant to gas-and-oxygen during a long dental operation, thus enabling the oxygen to be increased to 15% or even 20%, without affecting the patient's recovery. The safety of vinyl ether, together with the ease of administration, make it the most practical form of anaesthesia for the general practitioner who is called upon to give anaesthetics for short operations and does not possess the necessary apparatus for the administration of gas-and-oxygen.

Administration.—Vinyl ether, administered either by the open drop method or from a closed inhaler, will produce anaesthesia rapidly, giving an operative time of about a minute, and complete recovery in a further minute. Vomiting after administration has only occurred in three of our cases, and none of them has had to be detained for any post-anaesthetic complication. The open drop method of administration is the more convenient as only the container of vinyl ether and a mask are required, but greater quantities of the anaesthetic agent are used than in a closed method, and the induction is neither so certain, nor so rapid.

After a number of experiments a completely closed method of administration was adopted, and a special inhaler, which has been described in an earlier paper (Goldman, 1936), was devised to give rapid vapourization of the anaesthetic agent.

The inhaler (figs. 1 and 2) contains no valves, but only a simple method of adding vinyl ether to a sponge which is contained in a box placed between the face-piece and the rebreathing bag. Vinyl ether is distributed in ampoules of three c.c., as this quantity produces the required degree of anaesthesia for the average dental case, whether the patient is an adult or a child.

After the patient has been placed into position, and the prop inserted, the contents of an ampoule are shaken into the inhaler, and it is now my practice to inflate the bag partially in full view of the patient. This helps to gain his confidence, and vapourizes the vinyl ether. I have the considered opinion of Professor Webb of our Pathology Department, that the sponge acts as a mechanical bacterial filter, so that this practice is not so unhygienic as it appears. The inflated inhaler is

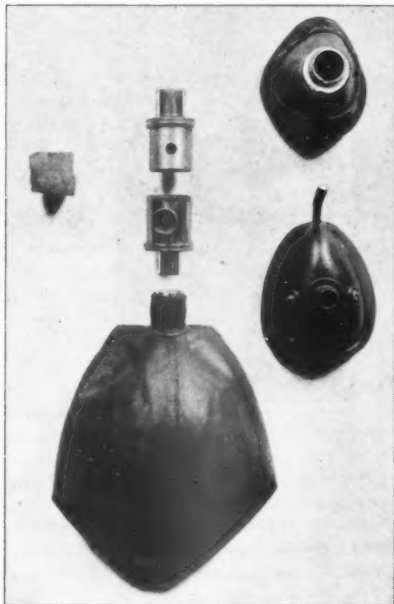


FIG. 1.—The parts of the inhaler.



FIG. 2.—The complete inhaler.

placed over the patient's face and he is instructed to breathe in and out. Although the smell of vinyl ether may be disagreeable to the surgeon and to the anaesthetist, patients do not complain. Within ten or fifteen seconds the face becomes slightly flushed, the conjunctivæ become suffused, and the eyes begin to water. In about fifty seconds anaesthesia is sufficient for dental operations; the eyelids usually remain open and the pupils do not, as a rule, dilate. The only reliable guide to the depth of anaesthesia is the onset of "automatic breathing". The mask is removed, a sponge or pack inserted, and the extractions can now be done. The cyanosis of gas anaesthesia is never seen, and except in exceptional circumstances, the patient remains a good colour throughout.

Vinyl ether may be added to gas-and-oxygen in several ways. The simplest way is to put it into the McKesson ether vapourizer, but this is extravagant, and without means of fine control. A better method is to fill the sponge-box of

the inhaler with 3 c.c. of vinyl ether and to plug it in between the ether vapourizer and the tubing when wanted. Further quantities of vinyl ether can be added as required. The most accurate method is by means of a drip feed, and fig. 3 shows how this can be fitted to most gas and oxygen machines. When adding vinyl ether to gas-and-oxygen it is an advantage to encourage rebreathing,

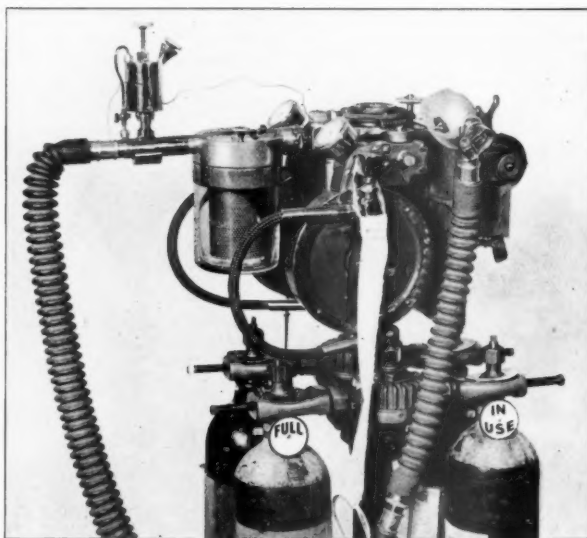


FIG. 3.—The drip attachment on a McKesson.

as this enables a high concentration of the vapour to be produced with economy, and it also gives the maximum effect of the adjuvant in the shortest time.

In conclusion I should like to express my thanks to the director of the Eastman Clinic, Mr. C. L. Endicott, for his assistance and encouragement, and to Mr. Daplyn for his co-operation in the taking of the film.

[A cinematograph film was shown.]

REFERENCES

- BOURNE, W. (1934), *Lancet* (i), 566.
 BOURNE, W., and RAGINSKY, B. B. (1935), *Brit. J. Anaesth.*, 2, 62.
 GOLDMAN, V. (1936), *Brit. M.J.*, 2, 122.
 MARVAN, F. W. (1935), *Anaesth. and Analg.*, 14, 257.
 MOLITER, H. (1936). Personal communication.
 SAGHIRIAN, L. M. (1936), *Dental Cosmos*, 5, 531.

Mr. C. L. ENDICOTT: During the past ten months I have seen vinyl ether administered to many patients and have been completely won over in regard to its suitability for short dental anaesthetics. I have never heard patients complain of the odour. I have formed the opinion that its particular indication is for use with infants and pre-school children. With this group of patients it possesses definite advantages over the other commonly used anaesthetics especially in the hands of anaesthetists with a limited amount of experience, and a more satisfactory anaesthesia is almost invariably obtained. Although its use is by no means limited to infants, it does not appear to possess the same advantages over nitrous oxide and oxygen for older patients.

Section of Psychiatry

President—T. A. ROSS, M.D.

[January 12, 1937]

Observations on Heredity in Neurosis

By R. G. McINNES, M.R.C.P.E., D.Psych.

No one who works with neurotic patients can fail to be impressed by the frequency with which a family history of nervous or mental disorder is given in these cases. I think it must be fairly general experience that the doctor engaging himself in this kind of work commences his career with a predominant orientation towards the importance of psychological explanations and the relief of symptoms by purely psychological means; and indeed with much justification, for at present these are almost the only specific instruments we possess which are practically effective. But, as experience is gained, I think the conviction grows that much of the neurotic problem lies neither in the nature of the symptoms nor in the manner of their production, but in the bare fact that under similar conditions some people suffer neurotic breakdown and others do not. In other words, the operation of a constitutional factor begins to engage the attention of the physician and to loom ever more large in his speculation.

Freud, in his New Introductory Lectures, says: "The neuroses are serious, constitutionally determined affections which are seldom restricted to a few outbreaks but make themselves felt as a rule over long periods of life or even through its entire extent. Our experience, that we can influence them to a far-reaching degree if we can get hold of the historically precipitating causes and the incidental accessory factors, has made us neglect the constitutional factor in our therapeutic practice."

Elsewhere in the same book he mentions a constitutional instinctual endowment and speaks of hormonal action as possibly supplying the quantitative variations of instinct which are encountered in the course of analytic work.

In all except those cases in which the exogenous factors have been overwhelming, the existence of some degree of constitutional predisposition is generally recognized. Of what it consists, how it is transmitted or acquired, we do not know. The manner of its operation we may be able to learn.

It was with such thoughts in mind that I began to survey the neurotic case material which passed through my hands in the Jordanburn Nerve Hospital, Edinburgh. In the course of these observations it was noticed that certain differences, which might be of importance, existed between the family histories of anxiety neurotics, hysterics, and normal people.

Fifty cases of anxiety neurosis, 30 cases of hysteria, and 75 controls, form the material of the investigation with which this paper deals.

The criteria for admission to the series were first, that an adequate account of parents and siblings should be available, and second, that the cases should conform to a more or less rigid classification. Unfortunately it was not found possible without the aid of field workers to obtain reliable family histories beyond the first degree of relationship, but in some respects this is an advantage. By this I mean that the family histories in all these cases were taken in the ordinary course of clinical work and before this investigation was thought of; this removes the possible objection that one finds what one is looking for. Furthermore, with a very few exceptions, the clinical histories and data from controls were taken by myself, a procedure which may make for uniformity. The family histories of the controls were, of course, taken later.

To begin, then, with an examination of the anxiety group. The clinical criteria for admission to this group were the occurrence of anxiety manifestations, consisting of palpitation, sweating, trembling, subjective feelings of fear, phobias such as claustrophobia, agoraphobia, &c., anxious preoccupation and the like. Cases showing conversion symptoms were not included, and likewise depressions with concomitant anxiety were not considered. Some anxiety neuroses show a mild secondary depression, however, which is commensurate with the disability and discomfort which the neurosis entails. Cases showing only this type and degree of depression, in addition to their anxiety symptoms, were not debarred from the series.

Of the 50 cases of anxiety neurosis 23 (i.e. 46%) had normal parents—that is to say, parents in whom no history of psychosis or neurosis was recorded. 14 (i.e. 28%) had one parent in whose case there was recorded a history of either chronic or occasional neurotic anxiety.

Where symptoms were recorded indicating the presence of anxiety sufficiently marked to give rise to spontaneous mention or to obvious objective manifestations, in that instance the relative was considered as a positive example of anxiety. The anxieties of the involutional type are not included in this conception.

In 14 of the 50 cases there was a history of anxiety in one parent.

Of these 14 cases :—

In 1 instance the other parent showed anxiety.

In 1 instance the other parent was asthmatic.

In 1 instance the other parent was melancholic.

Of the remaining 13 cases in whose parents, although no history of anxiety is recorded, yet some other abnormality existed—

8 gave a history of indefinite nervous disorder in one parent.

2 gave a history of asthma in one parent.

1 gave a history of hypochondria in one parent.

4 gave a history of alcoholism in one parent.

To recapitulate :—

In the parents of the 27 cases in which some parental abnormality was recorded there were—

15 instances of anxiety.

8 instances of indefinite nervous disturbance.

4 instances of alcoholism.

3 instances of asthma.

1 instance of melancholia.

1 instance of hypochondria.

Altogether in the whole anxiety group there were 2% cases showing psychosis and 34% of cases showing neurosis including 28% cases showing anxiety neurosis in the parentage. 18% showed a disorder too indefinite to classify (*see Table I*).

TABLE I.—PARENTS.

Illness	Percentage of cases showing psychosis in the parentage	Percentage of cases showing neurosis in the parentage	Percentage of cases showing neurosis or psychosis of similar type in the parentage
Anxiety neurosis ...	2	34	28
Hysteria ...	6.6	20	6.6
Controls ...	2.6	14.6	Anxiety 8 Hysteria 1.3

Considering now the siblings of this group of 50 cases of anxiety neurosis:—

In 25 (i.e. 50%) of the cases there was some abnormality in the siblings. In 23 (i.e. 46%) of the cases there was a history of neurosis or psychosis in the siblings; in 21 cases (i.e. 42%) neurosis, and in 2 (i.e. 4%) psychosis. Of these 21 cases, in 14 the siblings showed anxiety, i.e. in 28% of the total (*see Table II*).

TABLE II.—SIBLINGS.

Illness	Percentage of cases showing psychosis in siblings	Percentage of cases showing neurosis in siblings	Percentage of cases showing neurosis or psychosis of similar type in siblings
Anxiety neurosis ...	4	42	28
Hysteria ...	3.3	16.6	6.6
Controls ...	2.6	18.6	Anxiety 12 Hysteria 1.3

The total number of siblings of the whole group was 189. Of these 42 showed some neurotic or psychotic taint, i.e. 22%. Of these 28 were examples of anxiety, i.e. 14%.

Taking now the siblings of the 23 patients whose parents were normal. There was a total of 95 siblings. In these there were 3 examples of anxiety, 2 of melancholia, 2 of neurasthenia, 2 of mental defect, 2 of epilepsy, 1 of asthma, and 1 of chorea. This leads to the observation that in 23 families in which the parents were said to be normal, there were 36 out of 118 children with some taint, and of these 26, i.e. 22%, suffered in some degree from neurotic anxiety.

Considering now the 14 cases in which one parent suffered from anxiety, there were 68 siblings. Of these there were 18 examples of anxiety, 2 schizophrenics, 1 chorea, and 1 melancholia. This means that in 14 families in which one parent showed neurotic anxiety, 32 out of a total of 82 children, i.e. 39%, also showed neurotic anxiety (*see Table III*).

TABLE III.

	Anxiety group		
	Whole group	Those with normal parents	Those with anxiety in one parent
Percentage of siblings showing anxiety	14	3.15	26

Continuing the examination of this group of 14 cases in which one parent showed anxiety, and assuming for the moment that there may be some hereditary transmission, there were

- 18 instances of mother-daughter transmission,
- 9 instances of father-daughter transmission.
- 5 instances of mother-son transmission,
- 2 instances of father-son transmission.

Altogether, 23 instances of transmission from the mother, and 11 instances of transmission from the father. These figures agree in the main with Mott's findings for the psychoses in general.

The next part of the inquiry is concerned with a consideration of the possible effects of parental anxiety on the clinical course of the illnesses in the cases under review. The following table gives a comparison of the results :—

TABLE IV.—SHOWING THE EFFECT OF ABNORMALITIES IN THE PARENTAGE ON THE OUTCOME OF ANXIETY NEUROSIS.

Parentage	Percentage recovered	Percentage relieved	Percentage i.s.q.
Normal	43	47	8.6
One parent showing anxiety ...	42	42	14
Indefinite nervous disorder in parentage	30	53	17

A follow-up inquiry was made to render these results more valid. There was a large number of untraceables, and the smallness of the groups makes one hesitate to draw conclusions, but as far as the evidence goes it seems to indicate that there is no substantial difference in the outcome between the group with parental anxiety and the group which is free from it. On this basis one might argue that the presence of anxiety in the parents was not necessarily a bad prognostic factor, and vice versa.

It is a common observation that in taking the history of neurotic patients one frequently obtains accounts of previous symptoms of a neurotic nature. Many of these occur in childhood, and it seems that there might be some correlation between their presence at an early age and the presence of parental anxiety. It has to be remembered, of course, that nearly all children at one time or another may have fleeting fears—such as fear of strangers, fear of being alone, and fear of the dark, which, although essentially neurotic, are so universal as to be almost considered normal. The following figures do not include states of this kind :—

TABLE V.—SHOWING INCIDENCE OF NEUROSIS IN THE CHILDHOOD OF ANXIETY NEUROTICS.

	Parentage	
	Normal	Anxiety in one parent
Percentage of cases with neurotic or temperamental abnormality of any kind in childhood	60.8	64
Percentage of cases showing definite anxiety neurosis in childhood	48.5	50

Here, although there is a slight predominance of neurosis in the childhood of the group with anxious parents, it is not sufficiently marked, and the numbers are not large enough, to justify any conclusions.

I would like to consider now for a moment the question of causation. The assigning of causes in the anxiety states is difficult and depends, to some extent at least, upon the individual predilections of the physician. He may be definitely Freudian in his beliefs, or he may adhere to some other school of psycho-pathology, the teachings of which form the basis of this psychotherapeutic effort. It is beyond the scope of this paper to discuss these points, but I feel that psycho-analytic theory offers the only satisfactory explanation of mechanisms in the neurosis, and it has been my own experience that it provides a measure of understanding not attainable by other means, and without which psychotherapy tends to be irrational.

The theories of the therapist may not go so deep, however, and he may regard neurotic anxiety as simply the outcome of a disproportion between demand and capacity. Whatever be taken as the actual source of anxiety, however, it is a matter of clinical observation that certain situations, frequently related to the sex life of the individual, are prone to act as the apparent cause of what we clinically recognize

as anxiety neurosis. It may be that the nature of the precipitating situation has some relation to the occurrence of anxiety in the parentage of anxiety neurotics.

The following table sets forth the findings :—

TABLE VI.—SHOWING THE APPARENT CAUSES OF ANXIETY NEUROSIS.

Cause	Percentage Incidence of Causes		
	Parents normal	Anxiety in one parent	Indefinite nervous disorder in parentage
Marital incompatibility ...	26	7.1	7.6
Unsatisfactory intercourse ...	13	—	15.3
Masturbation ...	—	7.1	—
Coitus interruptus ...	8.4	21	30.7
Conflict over sex attachment ...	8.4	14.2	7.6
Separation from sexual object ...	8.4	28.4	7.6
Worry over illegitimacy ...	4.2	—	—
Influenza ...	4.2	—	—
Childbirth ...	4.2	—	—
War service ...	—	7.1	—
Oral sepsis ...	—	7.1	—
Domestic strife ...	8.4	—	—
Business worry ...	—	—	7.6
Failure of vision ...	—	—	7.6
No cause assigned ...	13	7.1	15.3

These figures are derived from numbers which are too small to justify conclusions. There is the suggestion however that those whose parents are neurotic are more likely to break down under sexual deprivation of a purely physical kind. On the other hand the well-endowed seem to be less able to stand general marital incompatibility.

The marked predominance of sexual causes is noticeable over the three groups.

Before leaving the consideration of the anxiety group I might mention that a comparison of the kinds of situations which give rise to anxiety in those with and those without previous manifestations yielded no definite differences. Further, in correlating the outcome of anxiety states with the occurrence of pre-neurotic symptoms we find that 33 out of 50 cases had shown previous symptoms.

Of these 42.4% recovered; 42.4% were improved; 15.2% were *in statu quo*.

Of the remaining 17 who showed no previous symptoms 47% recovered; 47% were improved; 6% were *in statu quo*.

The group without previous symptoms, therefore, shows slightly more favourable results.

HYSTERIA GROUP

Turning now to the second part of the investigation, namely the group of 30 cases of hysteria, I have to describe the criteria for admission to this group.

This is a difficult matter, and it would be impossible to give a comprehensive list of symptoms under this heading. In general, however, the cases in this group all showed conversion symptoms of some kind such as seizure, anaesthesias, paralysis, aphonia, and the like. In addition, there was in these cases an absence of anxiety amounting in some instances to the affective indifference generally supposed to be characteristic of the hysteric.

Of the 30 cases in this group :—

20 had parents in whom no abnormality was recorded,

10 had one or other parent in whom some abnormality was noted.

Of these 10 cases with one abnormal parent, there were :—

2 in which the parental abnormality was hysteria—6.6%.

2 in which the parental abnormality was anxiety neurosis,

1 in which the parental abnormality was epilepsy,

1 in which the parental abnormality was cyclothymia,

1 in which the parental abnormality was asthma,

1 in which the parental abnormality was stammer,

2 in which the parental disorder was indefinite.

These figures are perhaps too small to give significant percentages when considered by themselves, but in comparison with the previous anxiety group, it is to be noted that whereas 28% of the anxiety cases had one anxious parent, only 6.6% of the hysteria cases had a hysterical parent. The percentage of cases in which some form of neurosis occurred in the parentage of the hysteria group was 20 (see Table I, p. 25).

In considering the siblings of the hysteria group, it was found that the number of cases in which the siblings were abnormal was 7 out of 30. Of these, in 5 cases there was neurosis (i.e. 16.6%) and in 2 cases the siblings showed hysteria (i.e. 6.6%). In one case there was psychosis in the siblings (i.e. 3.3%).

Comparing these figures with the corresponding results for the anxiety group, we recall that in 46% of the anxiety cases there was neurosis or psychosis in the siblings, and that of these, 28% showed anxiety neurosis. The difference is perhaps sufficiently substantial to be noteworthy (see Table II, p. 25).

The total number of siblings in the hysteria group was 117. Of these 8 were recorded as having shown some abnormality. These were:

- 2 instances of anxiety neurosis,
- 2 instances of schizophrenia,
- 1 instance of melancholia,
- 1 instance of neurasthenia,
- 1 instance of mental defect,
- 1 instance of enuresis.

Four of these could probably be classed as neurosis, giving a percentage occurrence of neurosis in the siblings of this group of hysterics of 3.3.

In comparing these figures with those of the anxiety group, we find that there were 189 siblings, and of these 22% (as against 6.6%) showed neurosis or psychosis and 14% (as against 3.3%) showed neurosis of a similar type.

TABLE VII.—SHOWING THE PERCENTAGE INCIDENCE OF ANXIETY NEUROSION AND HYSTERIA IN THE SIBLINGS OF EACH GROUP.

	Anxiety group	Hysteria group	Controls
Percentage incidence of anxiety neurosis in siblings ...	14	1.7	4.5
Percentage incidence of hysteria in siblings ...	Nil	3.3	1.1

Considering for a moment the families involved in the hysteria group: There were 20 families in which no parental abnormality was recorded. In these 20 families there were 105 children (including the hysterics). These yielded 4 additional instances of abnormality, i.e. 24 out of 105, or 22.8%.

There were 10 families in which there was abnormality in one parent. In these families there were 42 children including the hysterics. These also yielded 4 instances of tainting, i.e. 14 out of 42, or 33.3%.

Again, these results are perhaps not particularly significant in themselves, but when it is remembered that the family histories were taken before such an inquiry as this was considered, that they were with few exceptions taken by one individual, and that there seems no reason to suppose that the informants in one group were more reticent or less accurate than in the other, the differences between the hysteria group and the anxiety group with regard to the occurrence of a neurosis of similar type in parents and siblings, is worthy of comment.

In the anxiety group it was found that in 36% of cases there was psychosis or neurosis in the parentage, and in 28% the neurosis was similar in type; while in the hysterics, in 26% of cases the parentage showed neurosis or psychosis, and in only 6.6% could the abnormality be said to be similar to that occurring in the patient (see Table I, p. 25).

In attempting to discover some correlation between the heredity of this group of hysterics and the outcome of the illness, the following results were obtained:—

TABLE VIII.

Parentage	Outcome of hysteria State on discharge		
	Percentage recovered	Percentage improved	Percentage I.S.Q.
Parents normal	30	45	25
One parent abnormal	30	40	30

On this basis there is no noteworthy difference in the outcome of the two groups ; in fact their similarity is noticeable.

As in the case of the anxiety group, an effort was made to determine in the hysterics the possible correlation between heredity and the occurrence of previous symptoms.

Taking first the group of 20 hysterics with normal parents, we find that in 8, no previous symptoms were recorded. In 12 of the cases, some previous abnormality was recorded. This represents a percentage of 60, as compared with a percentage of 60.8 in the corresponding group of the anxiety cases.

Further, it was noted that of these 12, four showed previous symptoms which were predominantly hysterical in type, i.e. a percentage of 20 as compared with a percentage of 43.5 of the anxiety cases where previous anxiety was noted.

Turning now to the group of hysterics in which one parent showed some abnormality, it was found that in 2 cases no previous abnormality was recorded.

In 8 of 10 cases in which the parentage was normal, some previous neurotic abnormality had occurred in the patient. This represents a percentage of 80 which compares with a percentage of 64 in the anxiety group with abnormal parents.

Although the groups are small, and on this ground there must be hesitation in drawing conclusions, the figures in both groups point to the greater occurrence of neurotic trends in children with neurotic or psychotic parents. This is, of course, in accordance with clinical impression, but the figures further suggest that anxiety neurosis shows a greater tendency to run true to type than does hysteria.

In pursuance of further study of the hysterical group an attempt was made to trace a possible relationship between the occurrence of previous neurotic manifestations and the outcome of the illness for which the patients were in hospital.

In the group of 30 hysterics, 20 had shown some previous symptoms. Of these : 6 recovered (i.e. 30%) ; 8 were improved (i.e. 40%) ; 6 were unchanged (i.e. 30%).

Of the remaining 10 cases with no previous symptoms : 5 recovered (i.e. 50%) ; 4 were improved (i.e. 40%) ; and 1 remained unchanged (i.e. 10%).

Again the groups are small, but the tendency is towards a more favourable prognosis in those cases without previous neurotic history.

To complete the investigation of the hysterical group and to make further comparison with the anxiety cases, a survey of the apparent causes of breakdown was made. Again it must be emphasized that the allocation of single formal causes in such a group of cases is a matter fraught with difficulty and open to criticism ; but again it can be claimed with some justification that there are certain situations or kinds of situations, involving either through soma or psyche, the emotional life of the individual, which are clinically observed to be the frequent apparent cause of neurosis and which can often be expressed in a phrase as the main factor in the precipitation of the illness. For example, it is common to find that jealousy of a brother or sister is the obvious cause of a series of hysterical seizures. The basis of the attitude of jealousy is, of course, another matter and would involve a theoretic discussion of psychopathology which is outwith the scope of this paper. The presenting emotional situation, therefore, is for present purposes of comparison, taken as the main cause of the illness.

In considering the hysterical group on this basis, the following facts emerge :—

Taking first the group of 20 whose parents were normal, we find that the causes were as follows :—

In 5 cases jealousy of brother or sister.

These figures are perhaps too small to give significant percentages when considered by themselves, but in comparison with the previous anxiety group, it is to be noted that whereas 28% of the anxiety cases had one anxious parent, only 6.6% of the hysteria cases had a hysterical parent. The percentage of cases in which some form of neurosis occurred in the parentage of the hysteria group was 20 (see Table I, p. 25).

In considering the siblings of the hysteria group, it was found that the number of cases in which the siblings were abnormal was 7 out of 30. Of these, in 5 cases there was neurosis (i.e. 16.6%) and in 2 cases the siblings showed hysteria (i.e. 6.6%). In one case there was psychosis in the siblings (i.e. 3.3%).

Comparing these figures with the corresponding results for the anxiety group, we recall that in 46% of the anxiety cases there was neurosis or psychosis in the siblings, and that of these, 28% showed anxiety neurosis. The difference is perhaps sufficiently substantial to be noteworthy (see Table II, p. 25).

The total number of siblings in the hysteria group was 117. Of these 8 were recorded as having shown some abnormality. These were:

- 2 instances of anxiety neurosis,
- 2 instances of schizophrenia,
- 1 instance of melancholia,
- 1 instance of neurasthenia,
- 1 instance of mental defect,
- 1 instance of enuresis.

Four of these could probably be classed as neurosis, giving a percentage occurrence of neurosis in the siblings of this group of hysterics of 3.3.

In comparing these figures with those of the anxiety group, we find that there were 189 siblings, and of these 22% (as against 6.6%) showed neurosis or psychosis and 14% (as against 3.3%) showed neurosis of a similar type.

TABLE VII.—SHOWING THE PERCENTAGE INCIDENCE OF ANXIETY NEUROSIS AND HYSTERIA IN THE SIBLINGS OF EACH GROUP.

	Anxiety group	Hysteria group	Controls
Percentage incidence of anxiety neurosis in siblings ...	14	1.7	4.5
Percentage incidence of hysteria in siblings ...	Nil	3.3	1.1

Considering for a moment the families involved in the hysteria group: There were 20 families in which no parental abnormality was recorded. In these 20 families there were 105 children (including the hysterics). These yielded 4 additional instances of abnormality, i.e. 24 out of 105, or 22.8%.

There were 10 families in which there was abnormality in one parent. In these families there were 42 children including the hysterics. These also yielded 4 instances of tainting, i.e. 14 out of 42, or 33.3%.

Again, these results are perhaps not particularly significant in themselves, but when it is remembered that the family histories were taken before such an inquiry as this was considered, that they were with few exceptions taken by one individual, and that there seems no reason to suppose that the informants in one group were more reticent or less accurate than in the other, the differences between the hysteria group and the anxiety group with regard to the occurrence of a neurosis of similar type in parents and siblings, is worthy of comment.

In the anxiety group it was found that in 36% of cases there was psychosis or neurosis in the parentage, and in 28% the neurosis was similar in type; while in the hysterics, in 26% of cases the parentage showed neurosis or psychosis, and in only 6.6% could the abnormality be said to be similar to that occurring in the patient (see Table I, p. 25).

In attempting to discover some correlation between the heredity of this group of hysterics and the outcome of the illness, the following results were obtained:—

TABLE VIII.

Parentage	Outcome of hysteria State on discharge		
	Percentage recovered	Percentage improved	Percentage I.S.Q.
Parents normal	30	45	25
One parent abnormal	30	40	30

On this basis there is no noteworthy difference in the outcome of the two groups ; in fact their similarity is noticeable.

As in the case of the anxiety group, an effort was made to determine in the hysterics the possible correlation between heredity and the occurrence of previous symptoms.

Taking first the group of 20 hysterics with normal parents, we find that in 8, no previous symptoms were recorded. In 12 of the cases, some previous abnormality was recorded. This represents a percentage of 60, as compared with a percentage of 60.8 in the corresponding group of the anxiety cases.

Further, it was noted that of these 12, four showed previous symptoms which were predominantly hysterical in type, i.e. a percentage of 20 as compared with a percentage of 43.5 of the anxiety cases where previous anxiety was noted.

Turning now to the group of hysterics in which lone parent showed some abnormality, it was found that in 2 cases no previous abnormality was recorded.

In 8 of 10 cases in which the parentage was normal, some previous neurotic abnormality had occurred in the patient. This represents a percentage of 80 which compares with a percentage of 64 in the anxiety group with abnormal parents.

Although the groups are small, and on this ground there must be hesitation in drawing conclusions, the figures in both groups point to the greater occurrence of neurotic trends in children with neurotic or psychotic parents. This is, of course, in accordance with clinical impression, but the figures further suggest that anxiety neurosis shows a greater tendency to run true to type than does hysteria.

In pursuance of further study of the hysterical group an attempt was made to trace a possible relationship between the occurrence of previous neurotic manifestations and the outcome of the illness for which the patients were in hospital.

In the group of 30 hysterics, 20 had shown some previous symptoms. Of these : 6 recovered (i.e. 30%) ; 8 were improved (i.e. 40%) ; 6 were unchanged (i.e. 30%).

Of the remaining 10 cases with no previous symptoms : 5 recovered (i.e. 50%) ; 4 were improved (i.e. 40%) ; and 1 remained unchanged (i.e. 10%).

Again the groups are small, but the tendency is towards a more favourable prognosis in those cases without previous neurotic history.

To complete the investigation of the hysterical group and to make further comparison with the anxiety cases, a survey of the apparent causes of breakdown was made. Again it must be emphasized that the allocation of single formal causes in such a group of cases is a matter fraught with difficulty and open to criticism ; but again it can be claimed with some justification that there are certain situations or kinds of situations, involving either through soma or psyche, the emotional life of the individual, which are clinically observed to be the frequent apparent cause of neurosis and which can often be expressed in a phrase as the main factor in the precipitation of the illness. For example, it is common to find that jealousy of a brother or sister is the obvious cause of a series of hysterical seizures. The basis of the attitude of jealousy is, of course, another matter and would involve a theoretic discussion of psychopathology which is outwith the scope of this paper. The presenting emotional situation, therefore, is for present purposes of comparison, taken as the main cause of the illness.

In considering the hysterical group on this basis, the following facts emerge :—

Taking first the group of 20 whose parents were normal, we find that the causes were as follows :—

In 5 cases jealousy of brother or sister.

In 4 cases physical and accompanying psychic trauma.

In 3 cases dislike of occupation.

In 1 case conflict over marriage.

In 1 case worry over defective child.

In 1 case trauma of sex assault.

In 1 case conflict over sterilization.

In 1 case fear of tonsillectomy.

In 1 case fear of responsibility.

2 cases in which no definite cause could be assigned.

In the group of 10 in which one parent was abnormal, the causes were :—

In 2 cases jealousy of brother or sister.

In 1 case dislike of occupation.

In 4 cases conflict over sex attachment.

In 1 case fear of pregnancy.

2 cases in which the cause was indefinite.

Although there is perhaps no very significant difference in the nature of these two groups, it is noteworthy that in the hysterical group as a whole, several situations appear repeatedly as assigned causes which have no place in the list of factors described in connexion with the anxiety group. In particular, the jealousy situation, which occurs seven times in a group of 30 hysterics, does not occur in relation to the anxieties at all. Similarly, dislike of occupation is peculiar to the hysterical group as a causal factor.

From this it might be argued that the nature of the apparent cause of breakdown tends to be less subtle in the hysteric than in the anxiety neurotic. This, I think, is in accord with clinical impression and particularly with the general belief that, on the whole, hysterics are of comparatively meagre intellectual endowment.

CONTROL GROUP

The third section of this survey is concerned with the control group. This consisted of 75 *propositi*, of whom 44 were females and 31 males, giving a relative percentage of 58.6 to 41.4.

In the anxiety group the relative percentages of females and males was 62 and 38, and in the hysteria group 83.4 and 16.6. As far as possible the conditions governing the investigation of the control group were made to correspond with those under which information relating to the parents and siblings of patients in the two previous groups was obtained. That is to say, the data was procured in the course of a personal interview with the *propositus* during which the nature and purpose of the investigation was explained and the co-operation of the individual invited. In order to facilitate confidence, the anonymous principle was emphasized and preserved.

The actual *propositi* were drawn partly from the staff of the Royal Edinburgh Hospital and partly from personal acquaintances of myself and my colleagues and friends. In this way a mixed group was obtained, corresponding in range of age, occupation, and social level, with the groups of patients suffering from anxiety neurosis and hysteria which formed the previous parts of this investigation.

Considering first the parents of the controls, it was found that in 54 out of the 75 *propositi* both parents were said to be normal, i.e. 72%.

Of the remaining 21 *propositi*, in 11 there was an account of neurosis in one parent, i.e. in 14.6% of the total, in 2 there was definite psychosis in one parent, i.e. in 2.6% of the total, in 8 there was an indefinite abnormal state, i.e. in 10.6 of the total; these were probably: 2 cases of asthma, 2 of cyclothymia, 2 of irritability of unknown origin, and 2 undefined.

It is to be particularly noted that the number of *propositi* in whose parentage neurotic anxiety was recorded was 6 (or 8%).

This is to be compared with the state of affairs relating to the anxiety neurotics in which, it will be recalled, 28% of the cases gave a history of neurotic anxiety in one or other parent. This difference is sufficiently large to be of some significance.

Of the remaining 5 cases in which neurosis was recorded in the parentage, there was only one instance in which the neurosis was hysterical in type, i.e. in 1.3% of the total (*see* Table I, p. 25).

In considering the siblings of the control group, it was found that the number of *propositi* in which the siblings were said to be normal was 53 out of 75 or 70.6%. The remaining 22 showed some abnormality in the siblings.

The number of *propositi* in which neurosis or psychosis occurred in siblings was 16 out of 75, or 21.3% (*see* Table II). This compares with a percentage of 46 for the anxiety group and 19.9 for the hysteria group.

It will be noted that this figure is lower than that for the control group. This is probably to be explained by the fact that in the control group the directed interest of the observer may have resulted in the more thorough discovery of family abnormalities. On this basis it might be suggested that the figures for abnormality in the control group are disproportionately high. If this is true, the differences between them and the figures for the other groups are probably less than that which exists in reality.

Of the 22 *propositi* in whose case there was some abnormality in the siblings,

In 2 instances the abnormality was psychosis (i.e. 2.6%),

In 14 instances the abnormality was a neurosis (i.e. in 18.6% of the total),

and in 6 cases the abnormality was too indefinite to classify (i.e. in 8%).

Taking the group of 14 *propositi* in which neurosis occurred in the siblings, it was found that in 9 of these the neurosis was of the anxiety type, i.e. in 12% of the total.

This figure is to be compared with that of 28% of the anxiety group, in which the siblings also showed anxiety neurosis.

In the case of 1 of the 14 *propositi* mentioned here, hysteria occurred in the siblings, i.e. 1.3% of the total, compared with 6.6% of cases in which hysteria occurred in the siblings of the hysteria group (*see* Table II).

The total number of siblings of the control group was 176. The incidence of anxiety neurosis in this group was 4.5%, as compared with 14% in the siblings of the anxiety group. The incidence of hysteria in the siblings of the control group was 1.1%, as compared with 3.3% in the siblings of the hysteria group (*see* Table VII).

Finally, taking the controls as a closed group by themselves, it was found that there were 251 children of 75 matings, giving a total of 401 individuals.

It was found that the percentage incidence of psychosis in the parents was 1.3, in the children 0.79, giving a percentage, over the total, of 1.

The incidence of neurosis appeared to be higher, i.e. 7.3% in the parents, 6% in the children, and 6.4% over the total, i.e. 64 per thousand.

This concludes the description of the data collected from the material investigated. For many reasons it would be unjustifiable to attempt to draw definite conclusions as to the possible hereditary transmission of anxiety states or hysteria. In the first place, the groups and subgroups are numerically small, although this defect is, to some extent, offset by the provision of controls. Apart from this, however, there is the difficulty at present of assessing how much of any constitutional neurotic tendency is genetically inherited, how much may be dependent upon intra-uterine toxic or other congenital factors, and how much is due to anomalies of libidinal development in infancy.

The last of these possibilities again introduces psycho-analytic concepts. At this point I must make it clear that, although it is the purpose of this paper to draw attention to the constitutional factor in neurosis, the intention is not thereby to minimize the great importance of the psychogenic factor, but rather to range the

two alongside each other in order to give a more balanced perspective of the neurotic problem.

It has been my experience that there are many cases of neurosis arising out of psychic conflict in which the patients appear to have *no* constitutional predisposition. In such instances, the conflict is generally intense and activated by powerful exogenous stimuli. Recent cases of this nature probably offer the best hope of recovery with psychotherapeutic help, and one embarks on their treatment with optimism. At the other end of the scale there are cases in which the patients have shown a consistent tendency to break down under ordinary or even trifling strains and in which the physician can only employ the simplest therapeutic procedures. In such cases I think it is justifiable to postulate the existence of a constitutional neurotic tendency. Between these two extremes there are all grades of combination of factors, and it is my own opinion that judicious treatment cannot be instituted until these have been assessed as far as possible and each given its due place in the causation of the neurosis.

The question arises as to what guides we have in reaching such an assessment, and it was with the idea of initiating a search for some standards, especially in relation to heredity, that this paper was written.

Newman and Carter have demonstrated in studies on normal twins the influence of germinal factors in the production of emotional variations.

The recent investigation of a series of manic depressive twins, by Rosanoff, Handy, and Plesset has thrown fresh emphasis on the importance of heredity in these conditions.

The survey with which the present paper deals furnishes confirmatory evidence of the general feeling that neurotic patients are more heavily loaded than the general population, and, in particular, it suggests that in anxiety neurosis there may be a specific hereditary factor or group of factors which operate in some cases in producing the emotional disorder. Much work of a more detailed and extensive nature is required before this point can be established, and this paper represents only a tentative approach to the subject.

I wish to express my indebtedness to Professor D. K. Henderson for permission to utilize the case material and for much valuable help and criticism, and to thank him and Dr. T. A. Ross, through whose kindness I was privileged to present this paper to this Section of the Royal Society of Medicine.

REFERENCES

- CARTER, H. D. (1935), *Character and Personality*, 4, 61.
FREUD, S. (1933), "New Introduct. Lct. on Psycho-Analysis", London, p. 197.
MOTT, F. W. (1910-11), *Eugenics Rev.*, London, 2, 245.
NEWMAN, H. H. (1935), *Am. Naturalist*, 67, 193.

Section of Otology

President—DOUGLAS GUTHRIE, M.D.

[March 5, 1937]

Labyrinthine Reactions and their Relation to the Clinical Tests

By W. J. McNALLY, M.D.

*Department of Physiology, McGill University, and Department of Otolaryngology,
Royal Victoria Hospital, Montreal.*

ABSTRACT.—The rapid tilt test has shown that the vertical semicircular canals are in close connexion with the whole postural body musculature. Nystagmus reactions are only a small part of semicircular canal sphere of control.

Further knowledge of the reaction-pattern of the body musculature resulting from the stimulation of each semicircular canal will help in diagnosing a lesion, not only of the individual semicircular canals, but also—even more important—of its intracranial connexions. The few reaction patterns already known, but not recognized as such, namely post-pointing, falling, and head turning, are true compensatory reactions, more easily understood if so considered and grouped with the protective reactions to the tilt tests.

Recognition of the two modes of utricular action is essential to a correct analysis of tilt test reactions. The slow tilt described by Grahe and others, is an excellent test for "first mode" utricular action, but not for "second mode" action or for vertical semicircular canals.

The quick tilt is primarily a test of vertical semicircular canal action, but normally the reaction is complicated by reactions from "second mode" utricular stimulation. If this fact is not taken into account the analysis of a reaction to a quick tilt may be misleading. When performing a quick tilt test, in addition to watching for the absence of the protective reaction (due to loss of one or both labyrinths), the investigator should try to note whether there is a tendency for the patient to be more easily thrown in the direction of the tilt—owing to a lesion of the vertical canals, the utricles being intact ("second mode" utricular action)—or whether there is a tendency for the patient to over-compensate (owing to a lesion of the utricles, the vertical canals being intact).

If, in addition to the usual equilibrium tests, the quick tilt test is used in this way and a careful analysis is made of the reactions of patients with labyrinthine or intracranial lesions, diagnosis of lesions of individual labyrinthine end-organs or of their intracranial connexions may become a routine procedure in the clinic just as it is now possible in the laboratory.

RÉSUMÉ: L'épreuve de l'inclinaison rapide a démontré que les canaux semi-circulaires sont en rapport étroit avec les muscles déterminant la position. Les réactions de nystagmus ne forment qu'une petite partie du domaine des canaux semi-circulaires.

MAY—OTOL. 1

Une connaissance plus grande des types de réaction musculaire produite par la stimulation des différents canaux rendra plus facile le diagnostic des lésions de chaque canal, et aussi—ce qui est encore plus important—de celles de ses communications intracrâniennes. Les quelques types de réaction que nous connaissons déjà, sans les reconnaître comme telles, c'est-à-dire les défauts d'indication, la chute, le tour de la tête, sont de véritables réactions de compensation, qui deviennent plus compréhensibles quand on les considère de ce point de vue et si on les inclue dans le groupe de réactions protectrices aux épreuves d'inclinaison. L'admission de deux types d'action utriculaire est essentielle pour l'analyse correcte des épreuves d'inclinaison. L'épreuve de l'inclinaison lente, décrite par Grahe entre autres, est une excellente épreuve de la fonction utriculaire du "premier type", mais pas pour celle du "deuxième type", ni pour celle des canaux semi-circulaires verticaux.

L'inclinaison rapide est surtout une épreuve de la fonction des canaux verticaux, mais cette réaction est normalement compliquée par d'autres, provenant de la stimulation utriculaire du "deuxième type".

Si ce fait n'est pas reconnu, l'analyse de l'épreuve de l'inclinaison rapide peut être trompeuse. En exécutant cette épreuve il faut remarquer non seulement l'absence d'une réaction protectrice (due à la perte de l'un ou des deux labyrinthes) mais aussi noter si le malade tend à être plus facilement renversé dans la direction de l'inclinaison (à cause d'une lésion des canaux verticaux, avec utricules intacts) ou tend à compenser d'une façon exagérée (à cause d'une lésion utriculaire avec canaux verticaux intacts).

Si l'épreuve de l'inclinaison rapide est exécutée de cette façon, en plus des épreuves ordinaires de l'équilibre, et si les réactions dans les lésions labyrinthiques ou intracrânielles sont soigneusement étudiées, le diagnostic des lésions des différents organes terminaux ou de leurs communications intracrâniennes, comme il est possible aujourd'hui dans les laboratoires, pourra devenir une affaire de routine dans la clinique.

ZUSAMMENFASSUNG.—Untersuchungen mittels raschem Lagewechsel haben gezeigt, dass die vertikalen Bogengänge mit der gesamten Haltemuskulatur des Körpers in engster Verbindung stehen. Nystagmus-Reaktionen stellen nur einen kleinen Teil des Wirkungskreises der Bogengänge dar.

Eine Erweiterung unserer Kenntnisse über die Reaktionsweise der Körpermuskulatur bei Reizung der einzelnen Bogengänge wird die Diagnose einer Läsion nicht nur des betreffenden Bogenganges, sondern—was noch wichtiger ist—seiner intrakraniellen Verbindungen erleichtern. Die wenigen schon bekannten aber nicht in dieser Weise aufgefassten Reaktionsarten wie Vorbeizeigen, Fallen, und Kopfdrehen sind richtige Kompensationsreaktionen; sie werden leichter verständlich, wenn man sie in dieser Weise auffasst und mit den bei Lagewechsel auftretenden Schutzreaktionen zu einer Gruppe zusammenfasst.

Die Erkenntnis, dass es zwei Arten von Funktion des Utriculus gibt ist unerlässlich für eine korrekte Analyse der bei Lagewechsel auftretenden Reaktionen. Der langsame Lagewechsel, wie er von Grahe und anderen beschrieben wurde, ist eine ausgezeichnete Funktionsprüfung für die "erste Art" der Utriculusfunktion, aber nicht geeignet für die "zweite Art" Funktion oder zur Prüfung der vertikalen Bogengänge.

Die Prüfung mittels raschem Lagewechsel ist in erster Linie eine Prüfung der Funktion der vertikalen Bogengänge, jedoch wird normalerweise diese Reaktion durch "zweiter Art" Reizung des Utriculus kompliziert. Wenn man diese Tatsache nicht berücksichtigt kann die Analyse der Reaktion auf raschen Lagewechsel zu irreführenden Resultaten führen. Bei der Anstellung einer Funktionsprüfung mittels raschem Lagewechsel sollte der Untersucher—abgesehen davon, dass er auf das Fehlen der Schutzreaktionen (Folge des Verlustes eines oder beider Labyrinthe) achten muss—sich bemühen festzustellen, ob eine Tendenz besteht, dass der Patient leichter in Richtung des Lagewechsels aus seiner Position geworfen wird (Folge einer Läsion der vertikalen Bogengänge, bei intakten Utriculi (utrrikuläre Aktion "zweiter Art")—oder ob der Patient eine Tendenz zur Überkompensation zeigt (Folge einer Läsion der Utriculi, bei intakten Bogengänge).

Wenn man, abgesehen von den üblichen Gleichgewichtsuntersuchungen, die Funktionsprüfung mittels raschem Lagewechsel in dieser Weise benutzt und die Reaktionen von Patienten mit Labyrinth- oder intrakraniellen Läsionen einer sorgfältigen Analyse unterzieht, so dürfte es möglich werden die Diagnose von Läsionen bestimmter Endorgane des Labyrinths oder ihrer intrakraniellen Verbindungen routinemässig in der Klinik zu stellen, so wie derzeit solche Diagnose im Laboratorium bereits möglich ist.

OUR present knowledge of labyrinthine function began with the contribution of Purkinje in 1825. The rotation test was introduced to the clinic about fifty years ago through the work of Kreidl, of James, and of Jansen. The caloric test is little more than twenty-five years old and was introduced by Bárány and brought to its present form by Kobrak. The rapid tilt test, first introduced as a clinical test by Tait and McNally in 1926, has not yet received the general recognition that it deserves.

THE RAPID TILT TEST

The idea of tilting an animal out of the horizontal plane about a horizontal axis has been recognized for some time as a means of testing labyrinthine function. The slow tilt is the common form, both in the laboratory and the clinic, and it is used as a test of otolithic function (Jones and Fisher, 1918, and Grahe, 1927).

Ewald (1892) and Andre Thomas (1898) found that, following the removal of one labyrinth, an animal could be upset to the operated side if the table upon which it stood was suddenly tilted towards the side of operation. The quicker the tilt, the more easy it was to upset the animal. The test was introduced for use in patients by us in 1926 (see Tait, 1926). Following a loss of one or both labyrinths, if the patient is placed upon a tilt-table, it is very easy to upset him by a quick tilt to the side of the absent labyrinth. If the lesion is bilateral a tilt in any direction will upset him. We showed conclusively that the absence of a protective reaction to a quick tilt is due to a lesion of the semicircular canals.

In 1931 and in subsequent publications we have given a full description of the parts of the labyrinth concerned in the response to a slow tilt, on the one hand, and to a quick tilt on the other. A slow tilt stimulates the utricles but does not stimulate the semicircular canals, and in response to a slow tilt the utricles elicit a compensatory reaction. A quick tilt stimulates the vertical semicircular canals to bring about a prompt compensatory reaction of the body musculature. This reaction still takes place in the absence of the utricles, but in the frog it tends to be slightly overdone. De Kleijn and Versteegh (1935) found the reaction still present after the removal of one utricle in the rabbit.

The utricles are also stimulated ("second mode") by a quick tilt, but they tend to throw the body in the direction of the tilt—an anti-compensatory reaction. This "second mode" reaction of the utricles tends to check and to tone down the reaction from the vertical semicircular canals.

The rapid-tilt test proved to be an excellent method for demonstrating lesions of the individual vertical canals. Both Breuer and de Cyon had noted that, following an experimental injury to a semicircular canal, there was an abnormality noticeable in the animal's movements, chiefly when the movement occurred in the plane of the injured canal. In spite of this however, previous to our introduction of the quick tilt test, the eye reflexes were the only ones generally used, either in the clinic or in the laboratory, as an indication of semicircular canal function, but now the whole system of body musculature has been brought into connexion with the semicircular canals. The tonic labyrinthine and neck reflexes so completely described by Magnus and de Kleijn were never associated with the semicircular canals.

Since our work was published, Rademaker and Garcin (1932) and de Kleijn and Versteegh (1935) have used the quick-tilt test in the laboratory and the clinic as a means of diagnosing a loss of one or both labyrinths. These authors report that if the lesion is unilateral and of long standing, it may be compensated for, so that the patient may respond equally well to a tilt to either side. We also have found this to be true. They confirm our conclusion that the reaction to a quick tilt is chiefly from the canals.

ELIMINATION OF INDIVIDUAL LABYRINTHINE END-ORGANS

By 1930 we had developed our operative technique to such a point that it has since been possible in the frog to carry out an uncomplicated severance of the nerves to any or all of the semicircular canals, the utricles, or the saccules. This has made it possible for us to push the analysis of labyrinthine function to a point not hitherto realizable.

MECHANISM OF SEMICIRCULAR CANAL STIMULATION

It has been proved conclusively by Maxwell and by Steinhausen in certain fishes, and by McNally and Tait in the frog, that a semicircular canal responds to rotation in only one sense. Ewald found in birds (and presumably it is the case in man) that a semicircular canal responds to movement in either of two opposite senses. The reasons for applying this supposition to man are that, following a unilateral destruction of the labyrinth, it is still possible to elicit nystagmus by turning the patient to either side. Furthermore, the hot or cold caloric test elicits in each case its own form of nystagmus, presumably from stimulating the same canal in opposite directions. Since the explanation of the caloric and rotation tests is based upon the theory of two-way response of each semicircular canal, we must for the present accept this, but it is well to keep in mind that there is experimental evidence to show that this rule does not apply throughout all the vertebrates. Since Steinhausen's experiments demonstrating the movements of the cupula in the live pike, it is generally admitted that endolymphatic flow is the adequate stimulus of a semicircular canal.

The horizontal canal is stimulated by rotation about a vertical axis. This does not alter the animal's relation to the gravitational field. The animal's head must be held level during the rotation, and to accomplish this the vertical semicircular canals and the utricles must be intact. A lesion of any of these structures immediately shows itself in some slight unsteadiness of the head, which results in vertical canal reactions being superimposed upon the counter-circling reactions.

Rotation about a horizontal axis, which is in most cases a simple tilt, is the adequate stimulus for the vertical semicircular canals. Movement about this axis does change the animal's relation to the field of gravity, so that the animal must readjust itself in order to bring its centre of gravity back within the base of support.

CHARACTERISTIC REACTION PATTERNS OF BODY MUSCULATURE

When a semicircular canal is stimulated, the response of the body musculature is always so directed as to return the body, head, and eyes to their original positions—the movement is compensatory. If a horizontal canal is stimulated, the reaction involves the musculature of both sides of the body in such a way that the animal tends to circle in the direction opposite to the turning. Stimulation of a vertical canal also involves the musculature of both sides in such a way that the body tends to be shoved towards the corner diagonally opposite to the one in which the stimulated canal is located, e.g. the right anterior vertical canal reaction tends to shove the body, head, and eyes, backwards and to the left. We have found that the musculature which participates in any one of these complex reactions is invariably the same. The flexors and extensors, the abductors and adductors, of both sides of the body are innervated in such a manner each time as to bring about the same pattern of movements characteristic of each individual canal. As soon as one learns to recognize the reaction pattern characteristic for each canal, it is very easy to tell which canal is being stimulated. Frequently more than one canal is being stimulated simultaneously and, of course, the resulting reaction pattern of the body musculature is a combination of the canal effects, but it is still possible to analyse the resulting

reaction and to determine which canals have played a part. It is this consistent and characteristic involvement of the body musculature following stimulation of any particular semicircular canal that must, we feel, eventually be recognized as having great clinical importance. When they have been studied in man and the differences which result from the erect posture and from superimposed reflexes (neck reflexes, &c.) have been analysed and recognized, the presence or absence of any one pattern in response to a rapid tilt, will serve as an indication of the condition of its initiating canal.

THE TWO "MODES" OF UTRICULAR STIMULATION

It was suggested at the beginning of this address that we had found the utricle in the frog to be affected by two kinds of stimulation, and that a different reaction is elicited to each. I should like to explain this a little more fully.

"First Mode" of stimulation.—In response to a slow tilt the utricle sets up a compensatory reaction of the body, head, and eyes. It is best shown in a frog from which all the canals have been eliminated, the two utricles remaining intact. If the tilting is slowly and smoothly carried out, the animal shifts its position so as to keep the head level and its centre of gravity well within the base of support.

"Second Mode" of stimulation.—If the frog with only utricles intact is given a quick tilt, there is a prompt movement of the head and body in the direction of the tilt—an anti-compensatory reaction which tends to upset the frog. This reaction is not present in a delabyrinthized frog, so it must arise from the utricular maculae. Because of the frog's natural squat position, the animal is particularly well adapted to bring out the unsteady effect of the second mode of utricular action. An animal which stands high on its four legs like a dog is more readily upset on a tilt-table, because its centre of gravity is more easily displaced outside the base of support. Because of this a delabyrinthized dog is very easily upset by a quick tilt in contradistinction to a delabyrinthized frog. How a dog with only two utricles would behave in response to a quick tilt would be a very interesting problem to investigate.

The difficulty of carrying out ablation operations on the individual end-organs of the mammalian labyrinth, together with the difference in posture as compared with the frog, are sufficient to account for the fact that the two modes of utricular action which we discovered in the frog have not been identified as yet in the mammal.

MECHANISM OF UTRICULAR STIMULATION

If a frog from which one labyrinth has been removed is very carefully manipulated, it can be made to assume a symmetrical pose for a considerable period of time. It requires a definite head movement, as from a jar of the table, before the characteristic asymmetrical pose is resumed. From this and other experiments it is quite obvious that the utricle is not constantly signalling and that it requires some slight movement or accentuation of otolithic stimulation to initiate utricular action. The mere holding of a position is a property of the muscular system with its receptors. When the utricle is stimulated it may break up the existing posture and dictate a new muscular set-up.

A downhill slip of the otolith is not the adequate stimulus of the utricle. This is shown in the first two of the following experiments.

When a frog is tilted through a certain angle on the tilt-table, its head describes an arc of a circle. The farther the head is distant from the axis of rotation, the longer is this arc. Theoretically, a rapid arc displacement of the head gives a possibility of relative translatory movement of the otolith upon its macula, which might conceivably constitute the effective stimulus. So far as ready elicitation of this

reflex goes, one finds, however, that it is a matter of indifference whether the rapidly tilted animal is near or far away from the axis. Moreover, whether the frog (with a certain compass direction) sits on this side or on that side of the axis, it always responds in the same way. These facts, of themselves, practically dispose of the supposition that effective stimulation involves a translatory displacement of the otoliths.

Maxwell's (1923) direct experiment on the actual utricular otolith should also be kept in mind. Having freely exposed, in the dogfish, a utricular otolith from above, he gently displaced it, backwards, forwards, or laterally, with the help of a light pledget of cotton-wool held in a forceps. To his surprise the effect of this displacement was exactly contrary to what might have been predicted on the Kreidl gravity hypothesis. For example, a forward displacement of the otolith, instead of making the eyes roll upwards, caused them to roll downwards, and so on.

Ulrich (1935) has also carried out experiments on the exposed utricular otolith. As a means of applying pressure, having exposed the utricular otolith in the live pike, he used a human hair held in a micro-manipulator. He also noted eye movements as an indication of utricular reaction. He found that the only effective pressures or movements of the otolith were those directed outwards and forwards, or directly outwards. Pressure inwards, or backwards, elicited no reaction of the eyes. Furthermore, when the eye on the side of the stimulated utricle reacted, it always moved upwards, and the opposite eye moved downwards. From any manipulation of the utricle he could not make the eye on the same side move downwards. Since his results are quite different from Maxwell's, he suggests that the pressure applied to the otolith in Maxwell's experiments was not so carefully measured as in his own. In view of Ulrich's findings, our experiments should be recalled, in which only one utricle is left intact in the frog, the remaining end-organs having been eliminated.

A solitary utricle is able to elicit normal reactions in response to a slow tilt backwards, forwards, or to either side. It is, however, more responsive to a lateral than to a medial tilt.

Ulrich's findings lessen the value of those of Maxwell as a support for any theory of utricular mechanism but they do not exclude any particular theory, since obviously both sets of experiments are technically extremely involved, and must be repeated before either can be accepted as an indication of what happens within the utricular chamber.

Our experiments have shown that there are not two different mechanisms of utricular stimulation. The utricular process corresponding to the "first mode" and to the "second mode" of stimulation is one and the same thing. We have made the tentative suggestion that if the otolith would tend to preserve, under the influence of gravity, a vertical orientation like that of a buoy floating in water, it would fulfil the necessary conditions to explain the two modes of utricular stimulation (*see* Tait and McNally, 1934).

The utricles have connexions with the same muscle groups as have the vertical semicircular canals. They are able to elicit the same reaction patterns of the body musculature. It is necessary, however, to distinguish between the two modes of utricular stimulation. In response to a quick tilt backwards the utricles (second mode) elicit the same reaction pattern of the musculature as results from a quick forward tilt of the vertical semicircular canals, and vice versa. On the other hand, a slow forward tilt of the utricles (first mode) elicits the same reaction pattern as a quick forward tilt of the vertical semicircular canals.

The reactions from the vertical semicircular canals and from the second mode of utricular stimulation are mutually opposed. The utricles tend to thrust the head and body in the wrong direction, while the canals tend to over-compensate for the

stimulus. The two, acting together, neutralize each other sufficiently to bring about promptly the exact amount of compensatory reaction necessary to overcome the exciting stimulus.

SACCULE

Ablation experiments carried out upon the saccular otolith and nerve have not been able to demonstrate any equilibrical function for the saccule. This has been shown by Laudenbach, Maxwell, McNally and Tait, and Huddleston in the frog; by Parker, Maxwell, von Frisch, and Ulrich in fish; by McNally and Tait in the rattlesnake; and by Versteegh in the mammal. These results have been confirmed by the study of action currents from the saccular nerves in fish by Ross and in the frog by Ashcroft and Hallpike and by Ross and McNally. These latter experiments have afforded evidence that the saccule is concerned with the reception of sound vibrations and therefore may be part of the hearing mechanism. Since its connexion as part of the equilibrical mechanism has not been established we do not take it into consideration in analysing any of the reactions which follow vestibular stimulation.

INTRACRANIAL CONNEXIONS FROM THE LABYRINTH

It has been difficult to demonstrate labyrinthine representation in the cerebral cortex. Penfield and Gage have reported that only rarely does stimulation of the temporal-lobe cortex during operation cause a sensation of movement or dizziness in the patient.

Spiegel carried out labyrinthine stimulation on animals. In one set he strychninized various parts of the cerebral cortex after the method of Dusser de Barenne, and in another he recorded the electroencephalogram during the stimulation of the labyrinth. He felt that the results pointed to labyrinthine representation in the ecto- and supra-sylvian gyri, which would, in man, correspond to the posterior part of the temporal lobe.

The value of the equilibrical tests in localizing intracranial lesions is lessened for the four following reasons:—

(a) The complexity of the internal wiring: The great number of connecting paths from the vestibular nuclei to the other parts of the central nervous system are still not known in detail. In view of this scant knowledge, some harm has been done in the past by otologists attempting a too-ambitious localization of intracranial lesions based upon insufficient or misleading evidence derived from the vestibular tests.

(b) The difficulty of carrying out ablation operations on the individual end-organs in the labyrinth: This has been partly overcome by our development of a special operative technique in the frog, and by Versteegh's operations upon the utricle and saccule in the rabbit.

(c) Lack of knowledge of the reaction-patterns of the body musculature characteristic of stimulation of the individual labyrinthine end-organs: Now that these have been definitely established by us in the frog, it is a matter of determining how they have become modified in man. Once this is established, their recognition by neurologists and otologists, coupled with carefully controlled correlation studies with operative and post-mortem findings, may serve to fill in some of the gaps in our knowledge concerning the intracranial pathways from the individual labyrinthine receptors.

(d) Inadequate tests for canal and otolithic function have hampered progress: It is hoped that judicious use of the quick tilt test as a means of diagnosing lesions of the individual canals and their association with the utricle, will eventually add to the value of the vestibular tests in intracranial localization. Grahe's slow tilt method is well adapted to the study of "first mode" utricular stimulation.

REACTIONS FOLLOWING THE VESTIBULAR TESTS

The labyrinth is so designed as to be stimulated by any movement of the head in space. The resulting reactions are compensatory and are intended to return the body, head, and eyes to their original positions. To bring about this result the necessary muscle-groups are stimulated and the sympathetic and parasympathetic nervous systems are notified to make the necessary preparations in the way of extra blood-supply for the muscles, nerves, &c., that will take part in the readjustment. In addition there is a message sent through to consciousness that the head has been moved.

If the labyrinth is stimulated by anything other than active movement of the head—as, for instance, when the fluid in the semicircular canals is artificially moved during the caloric test—the central nervous system does not discriminate between this and a true head movement, with the result that the stereotyped set of reactions are called forth to meet an emergency which has not arisen. It is like a false alarm to the fire department; the engines arrive, there is no fire, and the engines only obstruct the traffic, because they were not really needed. A message goes through to the central nervous system that the head has moved, but the eyes and bodily sensations inform the central nervous system that the head has not moved, and it is these contradictory messages which result in the sensation of dizziness. The sympathetic and parasympathetic readjustments result in excessive flushing, perspiration, and nausea. The compensatory muscular readjustment of the body and limbs occurs to counteract a movement which has not taken place, with the result that they set up movements in the opposite direction. These movements are the fall of the body, the turning of the head, and the past-pointing of the limbs.

The sensation of movement (the vertigo or dizziness) is always in the same direction as the quick phase of the nystagmus and in the direction of the supposed stimulating movement. The slow phase of nystagmus, the fall, the turning of the head, and the past-pointing of the limbs, all being compensatory, are in the opposite direction.

When considered in this light, it becomes clear that past-pointing, falling, and head turning are really compensatory movements just as much as are the protective movements which resist a sudden tilt and they also have the characteristic reaction patterns of the musculature, depending upon which end-organ is stimulated. The reaction patterns are slightly modified because of the erect posture of the patient. When a patient on all fours is quickly tilted, the arms resist by buttressing, just as do the forelimbs of a frog. When, however, man assumes the erect posture and is subjected to a quick tilt his arms can now no longer act as a buttress and they are used in the same way as the tight-rope walker uses his pole. They are moved about in the air to alter the centre of gravity and bring it over the base of support. This explains why the arms, which have been held out straight in front of the patient after a caloric or rotation test, are both moved to the same side and opposite to the direction in which the patient feels that he is falling, but in the same direction as the other compensatory reactions, such as the turning of the head, &c. The so-called "disc-thrower's position" is this same reaction modified because of the patient's erect posture. It is a characteristic pattern of response of the body musculature resulting from special stimulation of the labyrinth.

Rademaker and Garcin (1933), and de Kleijn and Versteegh (1935) have noted that in the presence of certain intracranial lesions, the protective reactions to a quick tilt, together with the past-pointing and falling after the caloric or rotation tests, may be present or absent independently of the eye nystagmus which follows the caloric or rotation tests. This is another indication of the close association which exists between these compensatory reactions which follow labyrinthine stimulation. It would also suggest that their paths are separate from the vestibulo-ocular paths for nystagmus.

The experiments upon which these remarks are based have been carried out in

association with Professor John Tait, Head of the Department of Physiology, McGill University, Montreal.

BIBLIOGRAPHY

- EWALD, J. R. (1892), "Physiologische Untersuchungen über das Endorgan des Nervus octavus" Wiesbaden.
GRAHE, K. (1927), *Ztschr. f. Hals- Nasen- u. Ohrenh.*, **18**, 411-422.
JONES, I. H. and FISHER, L. (1918), "Equilibrium and Vertigo", J. B. Lippincott, Philadelphia, 444.
KLEIJN, A. DE and VERSTEEGH, C. (1935), *Acta oto-laryng.*, **24**, Fasc. 1, 34-52.
MAXWELL, S. S. (1923), "Labyrinth and Equilibrium". Philadelphia and London.
MCNALLY, W. J. and TAIT, J. (1925), *Am. J. Physiol.*, **75**, 155-179.
Id. (1933), *Quart. J. Exper. Physiol.*, **23**, 147-196.
MCNALLY, W. J. (1931), *Tr. Am. Acad. Ophth.*, **36**, 282-305.
RADEMAKER, G. G. J. and GARCIN, R. (1932), *Rev. Neurol.*, Tome I, No. 4, 637-653.
Id. (1933) *Ibid.*, Tome II, No. 5, 566-579.
TAIT, J. (1926), *Laryngoscope*, **36**, 713, also *Tr. Am. Otol. Soc.*, 1926.
TAIT, J. and MCNALLY, W. J. (1934), *Phil. Tr. Roy. Soc.*, Series B, Biological Sciences, No. 513, 224, 241-286.
THOMAS, ANDRE (1898), *Compt. rend. Soc. de biol.*, Paris, Series 10, Tome V, 594-596.
ULRICH, H. (1935), *Pflüger's Arch. f. d. ges. Physiol.*, **235**, 545-553.

Discussion.—Mr. SYDNEY SCOTT said that he had not made observations on frogs but only on fishes and pigeons. One conclusion arrived at was that the retina of the trout was maintained in the same position in water relative to space, by the integrity of the labyrinthine reflexes, which kept the trout's window constant, whether the trunk or head were moved by water currents (with certain limits of course) either upwards, downwards, or sideways.

When the labyrinth of the trout was destroyed the reflex control movements of the eye-ball were lost, and the retina could no longer be maintained in the same constant relative position in space.

When the pigeon's labyrinths were destroyed, it failed in its attempts to pick up a grain of Indian corn from the ground, because the neck muscles over-acted, as in Dr. McNally's frog's when deprived of the utricle, and the pigeon, though it could see, pecked too far and missed separate grains of corn scattered on the ground. It had to feed from a cupful of corn. He had never succeeded in differentiating whether this form of inco-ordination was due to utricular or to canalicular defunction. Probably it was due to utricular loss. Human beings seemed capable of adaptation to destruction of one and of both labyrinths, but even after four years the pigeon failed to compensate sufficiently to enable it to feed naturally.

Apparently the slow and fast tilting tests could be applied with advantage in clinical investigation; he had long considered that the rotation tests could be overdone. In neurological cases, what was often desired was to ascertain the minimal stimulus necessary to prove the efficiency of the vestibular nerves. When rotated very slowly in a chair, only a few degrees, the normal person would know definitely whether he were being turned, say to the left or to the right. In certain lesions of the vestibular nerve one could slowly turn the patient round to an extent of 45° to 90° or more, without his knowing the direction or whether he was being moved. He had been wondering whether Dr. McNally had ever tested cases of Friedrich's ataxy by strong rotation stimuli. Some years ago, he, Mr. Scott, had examined two cases of that disease and strong rotation produced convulsive seizures. However, a few weeks previously, he had applied the test to another reputed case of Friedrich's ataxy, but this patient did not over-respond.

Mr. C. S. HALLPIKE said that his first question concerned the effect of caloric stimulation of the utricle. There seemed good reason to believe that in the case of the canals the end-organs reacted rapidly, but they also adapted rapidly: i.e. if a constant stimulus was steadily applied, responses ceased. But in the utricle the adaptation was relatively slow, and continued stimulation of the utricle would give a continued response. He therefore thought that the caloric stimulus in its later stages would tend to stimulate the utricle more than the canals. With regard to the canal end-organs he would have thought that their response would be more especially confined to the onset of the stimulus.

With regard to the planes of the utricular macula: in the case of the rabbit, de Bourlet had shown that it lay on the floor of the vestibule. He (the speaker) had looked at many sections of the human temporal bone, and his impression was that the utricular macula lay more towards the roof, at the front upper corner.

He asked how it was possible to assess the degree of a nystagmic reaction. In the

nystagmic reaction the eyeballs oscillated with a certain amplitude and for a certain time, but he thought these factors were not necessarily associated; in one case the eyeballs executed movements of small amplitude over a long time; in another, the amplitude was larger and the time short. What was the factor which should be chiefly considered in determining the degree of the reaction?

Dr. DE KLEIJN (Utrecht) said that if one wished to know something about the functions of different parts of the labyrinth, it was necessary to cut through the nerve connexions to the different parts, and Dr. McNally had so far been the only person to do that. The result was a realization that the functions of the different parts of the labyrinth were much more complicated than had previously been supposed. Versteegh had been able to show that after extirpation of the sacule no static disturbances appeared in mammals, and that after section of the utricular nerve the reflex resulting from position disappeared, and the reflexes corresponding to movement were present. Up to the present time there was no knowledge about the reaction of the utricle on movements because one could not cut through the nerves going to the different canals. He wondered whether Dr. McNally had made experiments on mammals, or intended to do in the future, because he was the only worker, so far, who had the capacity for carrying out these very difficult experiments.

Mr. F. J. CLEMINSON said that he would like to ask Dr. McNally about one small clinical point. When a patient presented himself complaining of vertigo he was asked to try to describe his sensations during the attack. When pressed to be exact he might say that he felt that he was being whirled round in spite of himself. Or he might describe his sensations as not those of rotation. He might feel a little "swimmy" when he righted himself from a stooping posture, on account of changes in the blood-pressure following the change of position. But in the cases of which he (the speaker) was thinking, the chief complaint of the patient was not feeling at all sure of his equilibrium; he had a general feeling of insecurity, as if the floor on which he was standing was moving or changing its level, and he feared he might fall. If asked in what direction, he replied that it might be to the right, or to the left, or anywhere. Since first reading the work in which Tait and McNally differentiated the various parts of the labyrinth, he (Mr. Cleminson) had always wondered whether this form of vertigo might not be due to utricular disturbance, as the patient experienced just the kind of vague uncertainty which the frog seemed to show on the film. Did Dr. McNally regard this as a reasonable suggestion?

Dr. PHYLLIS M. KERRIDGE asked whether Dr. McNally had carried out experiments on frogs which were unable to see. Dr. Bogue and herself were planning to make a film showing disturbances of equilibrium in blind children, not for research reasons, but for the instruction of medical students. The maintenance of a normal posture and the regaining of equilibrium after it had been disturbed were very difficult for blind children. Their physical instruction in the special schools was much on the lines of balance exercises for sighted children, and they were encouraged in the playground to follow pursuits involving balance-sense, such as roller-skating, skipping, and walking on stilts. She would like to know whether Dr. McNally could suggest exercises or motions calculated to indicate the use of muscle groups, such as he had described in his lecture.

Mr. H. V. FORSTER said that he would like to have information concerning the value of the labyrinth as an end-organ assisting in the maintenance of muscle tone, but more especially with regard to the cristæ of the semicircular canals. He had understood from recent experiments that after division of the canals in pigeons the dynamic function was permanently lost but the tonic function returned after the cristæ had recovered from the shock of operation.

With regard to Dr. McNally's observations on intracranial tumours, he was reminded, when asked, as an otologist, to assist a physician in the localization of cerebral tumours, that in clinical cases, as well as in experimental animals, tumours at a considerable distance from the pons and medulla might give rise to vestibular symptoms.

Mr. F. C. ORMEROD said he wished to raise two points. The first concerned the slow-tilting experiments. The reaction due to the macula of the utricle only came into play after the frog had been tilted to the extent of 45° by the slow method. He wondered what was the explanation of that; apparently there was a threshold of appreciation by the utricle.

The other point concerned the relative strength of the response to the ampullifugal and ampullipetal currents in the canals. In any pair of canals the movement of the fluid in a particular direction in either canal would give the same result, and it was said that in the horizontal canals the ampullipetal result was stronger than the ampullifugal. Could Dr. McNally confirm that? or was he able to estimate the difference in the results from the two kinds of currents? It was important, when performing rotatory tests on patients, to know from which labyrinth one was obtaining results, or what was the proportionate result from the two.

Dr. McNALLY (in reply to Mr. Sydney Scott) said that he had not investigated cases of Friedreich's ataxy. If a test was evolved whereby the site of intracranial lesions in the vestibular pathways could be determined, investigation of such cases would be more enlightening.

With regard to the simultaneous occurrence of diplopia and nystagmus in some types of lesion, he had observed some cases of it.

In reply to Mr. Hallpike with reference to the adaptability of the canals as compared with that of the utricles, and the possibility of caloric effects on the utricles, he was prepared to accept Mr. Hallpike's explanation. The caloric was a splendid clinical test, but not much was known as to how it operated. Until the point was reached at which individual end-organ lesions could be produced in animals and caloric tests then carried out, one would not be able to say what was the labyrinthine effect of the caloric test.

He was unable to answer Mr. Hallpike's question as to the planes of the utricles; he had not had the pathological experience with the human subject that Mr. Hallpike had had.

Concerning measurement of the degree of nystagmus: In experimenting on frogs, not much time was spent in looking for nystagmus, and he had never been much impressed by the large amount of work which had been expended on attempts to differentiate fine degrees of it. So little was known about the tests that not much could yet be done in interpreting results. He had only done a little clinically in this matter, by observations on patients; frankly, he did not see that much could be gained in that way at present.

He much appreciated what Dr. De Kleijn had said about the second mode of testing in mammals. He (the speaker) had worked entirely with frogs in these researches. If the labyrinth of the frog was removed and it was placed on the tilt table, its body was wet, and hence it had a fairly firm setting, and when it was tilted, nothing happened, because the equilibrium was fairly well established; it was difficult to dislodge its centre of gravity from its basis of support. But mammals would be standing on four legs and their centre of gravity was high, so that in their case it was a simple matter to displace the centre of gravity. A de-labyrinthized man might be much more easily upset than was a frog after the same operation, therefore the second mode of stimulation was not so obvious, and that was why it was more difficult to detect. He was hoping that Dr. De Kleijn would himself carry out the investigations which would afford an explanation on these points; no one was better qualified.

He had been interested in Mr. Cleminson's idea and in the type of vertigo he mentioned. If only the utricles were attacked the patient was very wavy, and possibly he had an intracranial tumour or some type of lesion which picked out the utricular fibres and stimulated them. The floating sensation might be interpreted as an irritation of vestibular fibres in the brain stem.

In answer to Dr. Kerridge: All the frogs used in the experiments were first blinded by cutting both optic nerves; before this method was adopted the frogs were skittish at the first touch, and reactions occurred because of the use of the eyes. With regard to blind children, he thought that, from the scientific standpoint, the inclusion of some children who were blind and deaf would be valuable, because some of those who were blind with perfect labyrinths, would show certain reactions, while if both blindness and deafness were present, some other interesting reactions might be observed.

In reply to Mr. Forster: The crista probably had something to do with posture. It was believed that following some lesions the posture was normal, but this was not quite the case; there was a decannulated posture. What had been said about implanting tumours was not confirmed by his experience. It was amazing how little disability followed removal of large cerebral and cerebellar areas; one would not expect equilibrium to be affected unless the lesions were in the posterior fossa.

In answer to Mr. Ormerod: He had analysed carefully the slow-tilting test, and there was no rule which he could lay down. In the rotation tests he had found that in the lower animals only the maximum held. He hoped that some day more would be known about the caloric test and the rotation test, and what part was played by the factor of intracranial adaptation, so that maxima and minima could be discarded.

The following case was shown:—

Massive Involvement of Skull in Temporal and Occipital Regions by Carcinoma derived from a Rodent Ulcer.—JOHN F. SIMPSON, F.R.C.S.

Male, aged 65.

A "sore place"—probably a rodent ulcer—appeared in the region of the lower end of the right post-auricular groove in 1908 and in 1914 was treated by surface application of radium. The condition healed, and remained healed until early in 1934, when there was a small ulceration on the lower part of the pinna and adjoining the mastoid area. Deafness and aural discharge were noticed at this time. X-ray examination showed the mastoid to be largely eroded.

June 1934: Patient referred to Mr. Stanford Cade who irradiated the involved area as follows: 25.6.34: Interstitial needling, 2,034 mgm.-hrs.; 7.7.34: Surface application, 2,080 mgm.-hrs.

August 1934: All ulceration healed; no discharge from ear.

December 1936: Patient complained of pain in neck and shoulders (rheumatism) and very slight occasional serous discharge from ear. No ulceration behind the ear and no glands palpable. The introduction of a speculum into the contracted meatus caused bleeding.

January 1937: Intrameatal biopsy revealed "squamous-celled carcinoma, probably derived from a rodent ulcer" (Dr. W. Newcomb).

X-ray examination shows erosion of the posterior part of the petrous, the entire mastoid and part of the squama, also portions of the occipital and parietal bones.

There are no nerve palsies and the patient is still playing golf, quite unaware of the true condition.

The patient is now undergoing a course of tele-radiation given by Mr. Stanford Cade, who is employing the 4 gramme radium bomb.

Section of Laryngology

President—LIONEL COLLEDGE, F.R.C.S.

[March 5, 1937]

Unilateral Choanal Atresia in a Woman, aged 23.—T. B. JOBSON.

The patient had noticed obstruction of the right side of the nose and some discharge; otherwise she was perfectly healthy. Pharynx normal. She had reached the age of 23 without appreciating the fact that she could not in the slightest degree blow through the right nostril, although she could easily blow through the left.

On examination.—Right nostril full of muco-pus. Transillumination clear. At first a foreign body was suspected but on passing a probe a complete bony wall was found closing the choanal opening.

Discussion.—HERBERT TILLEY said that his personal experience of this form of posterior choanal atresia was limited to three cases. In the first patient the central portion of the diaphragm was membranous and was easily punctured by an antral trocar and the bony margins were enlarged by suitable bone forceps, but in the course of a few months the choana became entirely occluded again. The late Sir Charters Symonds suggested that, in order to prevent such post-operative stenosis, the median or vomerine border of the choana should be freely removed. This suggestion was adopted in the second and third patients, and the results left nothing to be desired.

SYDNEY SCOTT said he had seen only five cases of the kind. The first, many years ago, was bilateral, in a child. The surgeon pierced the membrane which occluded the posterior choanae, but removed no bone, and recurrence of obstruction took place. The second case was in a child under his own care, and he removed the posterior part of the vomer with a small Ostrom's punch; the procedure was successful. Another case was one that he had seen for the late Mr. Rose at St. Bartholomew's Hospital, and this had been treated in the same way, as had the fourth case seen more recently at the same hospital. The fifth case was in an infant who died within a few days of birth, without operation.

L. GRAHAM BROWN said that during the past year he had dealt with two cases of unilateral occlusion. The first was in a woman of about the same age as Mr. Jobson's patient. He performed the same operation as Mr. Tilley, but he allowed the patient to wear a rubber tube for five or six days. She had done very well. The other case was that of a child, aged 3, in whom the prominent symptom was suppuration. It was necessary to deal with the infection in this case, and at that age it was difficult to use forceps in the posterior region of the nose. He used as perforator a frontal sinus rasp which sufficed.

J. F. O'MALLEY said that an interesting aspect of this case was concerned with the physiology of the nose. To demonstrate that no air was going through, he used a tambour, and that showed that movement of air was absent on the right side. Another interesting problem was presented by the temperature in the nose on both sides. In the normal side it was under 94° F., on the other it was 98°. A further point of interest was the scavenging of the antrum. He suggested that Dr. Jobson should inject lipiodol on both sides and then compare by X-rays the rate of escape. That would throw some light on the question of how much the scavenging was due to the activity of the cilia alone, or to currents produced by variation of air pressure in addition.

MAY—LARYNG. I

C. A. SCOTT RIDOUT said that he had shown at a previous meeting a patient aged about 19, who had double congenital posterior choanal atresia.¹ The chest measurement was under the average. The operation of which Mr. Tilley had spoken was carried out and the patient thereafter breathed clearly. The turbinates were very corrugated, and the patient had no sense of smell; he had never had suppuration or a cold in the head.

T. B. LAYTON wished to point out that when these patients with double congenital atresia of the choana came to adult life they had perfectly developed facies and palates. Why operate on them during childhood when operations on the back of the nose were very difficult? It was better to wait until adult age when, if symptoms were present, a more satisfactory operation could be carried out. He asked whether anyone had seen a skull with bone in the posterior choana, or a soft specimen with this deformity, or had heard of any anatomist who had heard of such a condition. If so, where did the bone come from? Was it part of the vomer, or from some other part of the skull?

T. B. JOBSON (in reply) said that he had brought the case because the condition was uncommon. Stewart, of Edinburgh, had published in 1936 an account of similar cases, and stated that there had been only six cases during twenty years at Edinburgh Royal Infirmary. He himself had had only one case in eighteen years.

The Effect of Deep X-ray Therapy in a Case of Carcinoma of the Hypopharynx and Cervical Glands

By W. J. McNALLY (Montreal)

A. J., male, aged 52, first noticed shortness of breath in February 1935. He continued his work as a teamster until April, when he developed hoarseness and difficulty in swallowing. In May he noticed a swelling on the left side of his neck. He became bedridden in June and was admitted to the Royal Victoria Hospital, Montreal, on July 29, 1935.

Condition on admission.—He weighed 120 pounds, having rapidly lost about 15 pounds. He looked older than his stated age. He suffered from dyspnoea and stridor, and became comatose shortly after admission. There was a hard glandular mass on the left side of the neck, about 6 cm. in diameter. The nose and ears were normal. Patient was edentulous. In the left hypopharynx a mass, 2 cm. in diameter, filled the pyriform sinus. The surface was ulcerated and covered with a greyish exudate. This mass involved the left aryepiglottic fold and lateral pharyngeal wall. The epiglottis, which was infantile in type, was displaced to the right and overhung the larynx. It seemed to be the cause of the respiratory obstruction. The vocal cords could not be seen. The clinical diagnosis was made of a malignant growth of the left pyriform sinus.

A low tracheotomy was performed as an emergency measure, and following this, the general condition improved after a few days. The Wassermann reaction was negative. A direct laryngoscopic examination confirmed the above description of the growth. Sections of the biopsied tissue showed squamous-cell carcinoma with extensive necrosis and without keratinization.

Treatment.—Operative treatment was not considered advisable because of the extensive involvement of the pharyngeal wall and the cervical glands by the growth. After consultation with the radiologist (Dr. A. H. Pirie), it was decided to apply deep X-ray radiation after the method of Coutard. This treatment was begun on August 7, 1935, about a week after admission. Twenty-five daily treatments were given in the neck region. Each was equal to an epilation dose, or 250 r (with 200 kv., 5 ma., at 16-in. distance; filter $\frac{1}{2}$ mm. copper and 1 mm. aluminum). The patient had, in all, 3,250 r to the left side of the neck and 3,000 r to the right side.

¹ *Proceedings*, 1928, 22, 159 (Sect. Laryng., 3).

Result.—During the treatment the glands on the left side of the neck suppurated and had to be drained. It was feared that this suppurating mass might interfere with the efficacy of the radiation but the treatment was continued.

A direct laryngoscopy, October 1, 1935 (about a month after completion of treatment) showed the mass in the pyriform sinus to be greatly reduced. The sinus on the left side of the neck had closed and the glandular mass was reduced to a quarter of its size on admission. The tracheotomy tube was removed and the patient was discharged much improved. Unfortunately, the chest was not examined by X-rays.

Subsequent history.—A direct examination of the larynx on November 7, 1935, showed slight thickening of the epiglottis, but there was nowhere any evidence of growth or of ulceration. There was still some thickening of the tissues on the left side of the neck.

The patient was not seen again until September 1936. He had been fairly well until July 1936, when he developed a persistent dry cough and a dull pain in the left chest. He came to hospital September 1936, and was found to have a diffuse consolidation of the left lung. Clinical investigation, including a skiagram of the chest, led to the diagnosis of malignant tumours in both lungs and a diffuse left-sided pneumonia.

Local condition.—The hypopharynx was normal in appearance. The infantile epiglottis was pulled slightly to the left. The aryepiglottic folds on each side were normal. Both pyriform sinuses were normal. The vocal cords moved freely. There was no evidence of the original growth in the throat. The skin of the neck showed marked telangiectasis as a result of the X-ray treatment. The tracheotomy wound was firmly healed. The skin over both sides of the neck was soft and freely movable. There were a few small firm nodules palpable on the left, but these could not be considered as enlarged glands.

He recovered sufficiently from the pneumonia to be discharged to a convalescent home on October 19, 1936. He was fairly well for a few weeks, and then contracted left-sided pneumonia again. He came to hospital extremely ill on December 5, 1936, and died on the following day (fifteen months after completion of the deep X-ray treatment).

Post-mortem findings.—Local: There was no evidence that there had ever been a growth in or about the pharynx and larynx (see illustration, p. 44). The left pyriform sinus was slightly narrower than the right, but it was impossible to make out any gross induration, scar, or mucosal defect.

A soft grey tumour mass, resembling new growth, filled the lumen of the left lower lobe bronchus in its second and smaller divisions. This replaced the bronchial wall and fused with a solid grey granular cut surface which involved the left lung. Thick purulent material exuded everywhere, so that the tumour could not be differentiated from the partly organized exudate. As might be expected, there was evidence of a recent fibrinous and an old pleurisy on the left side and a recent fibrinous pericarditis. A few small, firm, grey nodules were found in the right lung and in the right lobe of the liver. Lymphogenous tumour invasion was traced from the peribronchial glands to the peri-oesophageal, gastric, and portal lymph-glands.

HISTOLOGICAL SUMMARY

Left pharyngeal region.—Several sections from the region of the pyriform sinus were examined. These showed a margin of stratified squamous epithelium with a flat intact basement layer. Beneath this, numerous glands showed partial atrophy. The fibrous connective tissue layer showed loss of nuclei and irregular shrinkage and concentration of the remaining nuclear material. There was hyaline fusion of collagen fibrils. There were few vessels and no budding capillaries could be seen. No definite tumour cells were found.



The left pyriform sinus is slightly narrower than the right, otherwise nothing remains to indicate the site of the tumour. The suture line in the post-cricoid region indicates where the larynx was opened at the post-mortem examination for inspection of the interior.

Left cervical and mediastinal glands.—Numerous sections showed a variable degree of prominence of large pale reticular cells and a relative loss of small lymphoid cells. This was more marked in the cervical glands. The surrounding fibrous connective tissue showed the atrophic changes described above. There were no tumour cells found.

Left lung and lower bronchus.—All bronchial coats were invaded and mostly replaced by a mass of immature polymorphic epithelial cells. In some places the tumour cells were irregular columnar and had a slightly glandular arrangement, while in others they showed a metaplasia to immature pavement epithelium and formed solid cell masses. There was extensive direct invasion of the lung tissue and tumour cells filled some lymphatics and some of the small blood-vessels.

Right lung, liver, and regional lymph-glands.—Sections showed a neoplastic picture similar to that described in the left lung and bronchus. Cells resembling immature squamous epithelium predominated.

ANATOMICAL DIAGNOSIS

X-ray scarring of the left peripharyngeal tissues, and of the integument of the left side of the neck (without carcinoma cells). Polymorphic carcinoma of the left lower bronchus, with direct extension to the lung and peribronchial glands; metastases in the lower œsophageal, gastric, and portal glands, and in the right lung and liver.

A generalized septicæmia was the immediate cause of death.

COMMENTS AND SUMMARY

(1) A malignant growth in the hypopharynx and cervical glands, which was considered inoperable, was destroyed by deep X-ray radiation, and the patient was freed from most distressing throat symptoms during the remaining fifteen months of his life.

(2) The above result is sufficient to justify deep X-ray therapy in a similar case even though an inaccessible growth in some other part of the body may prove fatal.

(3) In spite of the fact that suppuration occurred in the cervical glandular mass during the course of the deep X-ray radiation, there was a disappearance of the growth both in the hypopharynx and in the cervical glands. It is suggested as possible that the suppuration and discharge from the neck wound may have removed some of the necrotic malignant tissue which had been partly or completely destroyed by the X-ray therapy.

(4) When a malignant tumour has been located in any region, a thorough clinical search for tumours in other tissues and organs is indicated. The frequency of metastases, as well as the occurrence of multiple tumours (which are morphologically quite different) in the same patient, are well-recognized features.

(5) The question of cure cannot be considered in this instance, but the gross and microscopic absence of tumour cells in many histological sections of the neck tissues is noteworthy.

This case is one of a series included in a preliminary report of the results of treatment by deep X-ray therapy in twenty patients, by D. M. MacRae and A. H. Pirie, which will be published shortly. For the pathological report in this case, I am much indebted to Doctor W. H. Chase, assistant pathologist of the Royal Victoria Hospital and lecturer in pathology at McGill University.

Discussion.—THE PRESIDENT said that this case raised the question whether irradiation produced metastatic deposits; they seemed to occur frequently in cases in which the primary growth disappeared and did not recur. On the other hand secondary metastatic deposits were rarely seen in cases which went on for a long period after excision; if these succumbed later it was generally to a local recurrence. He mentioned one case which was treated by radium. The growth had been too far advanced to be dealt with by laryngofissure, and excision of the

larynx was contra-indicated because the patient had old hemiplegia. The result of the treatment by radium was locally perfect, but the man died of secondary deposits in the liver and lungs in less than two years. That was very rare with carcinoma of the larynx.

W. A. MILL agreed with the President's remark that radium therapy drove the carcinoma cells far from the primary growth. In a number of cases, especially those treated by radium bomb, which he had followed up, that had been the case.

W. J. McNALLY (in reply) said that no attempt had been made to treat the secondaries in the chest.

With regard to irradiation following operation, he asked the President whether he approved of following laryngofissure or laryngectomy by a course of deep X-ray therapy. Did he think that this would disseminate any possible growth, or that it would be a protective measure?

THE PRESIDENT, replying to Dr. McNally, said he was now against following laryngofissure by deep X-rays, as the results of this treatment of recurrences had been uniformly bad. His advice was, if it was proposed to combine surgery with irradiation, that irradiation should be employed first, then, when the skin had healed, the operation should be performed. Apparently there was no hope that the few remaining cancer cells might be killed by means of post-operative irradiation.

Basal-celled Carcinoma of the Palate.—W. A. MILL.

Male, aged 49.

History.—Admitted to the Royal Cancer Hospital in the summer of 1936 complaining of a swelling of the roof of the mouth, involving practically the whole of the hard palate, but more marked on the right side, expanding the right alveolus and causing some swelling in the right side of his cheek. A skiagram showed irregularity and bone absorption of the right maxilla. The first section taken was reported as a mixed salivary tumour. It was hoped that the tumour might be shelled out, but, owing to infiltration, this proved impossible. Examination of a further microscopical section resulted in the diagnosis of adenocystic basal-celled carcinoma. It was decided to see the effect of radium bomb treatment and 91 grm. hours were given. The tumour was very much reduced in size but did not by any means disappear. In November the right hard palate and tumour were removed and the walls treated with diathermy. An obturator was made and radium inserted into it, the dose given being 1,150 mgm. hours.

J. F. SIMPSON said that he had had a similar case in a woman with a "parotid tumour" in the palate. In 1935 she was treated by radium, and the growth appeared to subside. Later she suffered from deafness; it was a catarrhal deafness, because the nasal septum had become involved and was splayed out, as the palatal tumour took on a malignant change. He had removed the tumour, and at present the patient was well.

JOINT DISCUSSION No. 3

Section of Laryngology and Section of Anaesthetics

Chairman—LIONEL COLLEDGE, F.R.C.S. (President of the
Section of Laryngology)

[February 5, 1937]

**DISCUSSION ON THE CHOICE AND TECHNIQUE OF
ANÆSTHETICS FOR NOSE AND THROAT OPERATIONS**

T. B. Layton : We may consider surgery from three aspects—that in which every operation is done under general anaesthesia unless there is some reason against it, that in which every operation is done under local anaesthesia unless some factor prevent it ; it is better with balanced judgment to stand between these two.

In operative measures in the field of the upper respiratory tract we must add the special principle of the guarded larynx to the general principles which are common to the whole body. Of these one is that we should see what we are doing. Local anaesthesia, with its attendant haemostasis, is the only method that secures this in the nose. Another is that the area upon which the operation is being performed should be at rest. The pharynx therefore remains an area for general anaesthesia. Tonsillectomy and oesophagoscopy are examples. Examinations and operations through the direct laryngoscope come in the same category because the contact of the instrument on the tongue sets up movements that are uncontrollable under local anaesthesia. The exception is the removal of diphtheritic membrane from the larynx when the general condition of the patient contra-indicates any anaesthetic.

I think these exhaust the operative measures in which a general anaesthetic is necessary. All bronchoscopic work demands local anaesthesia.

I have watched experts perform operations on the neck both by a general and by a local technique, and have seen the work done beautifully by both methods. I believe that, with the exception of the block dissection of glands, the future of this branch of surgery lies with local anaesthesia.

I turn to premedication. Morphia combined with scopolamine in local anaesthesia has the advantage that the patient can be roused by the firmly spoken voice, and that when roused, control persists. Being an antidote to cocaine, morphia is a protection rather than a danger.

With general anaesthesia we have to weigh the increased risk from the administration of the drug against the advantage to be gained by premedication. Morphia seems best to hold this balance. The increase of risk appears to be the least, and the patient comes into the theatre in a comfortable state without the deep stertorous sleep of the other drugs. The barbiturates appear to add most to the risk. Avertin is between the two. The chief problem is whether there is any need for premedication with general anaesthesia. With local anaesthesia it is needed to neutralize the unpleasantness of the manual manipulations during the operation ; with general anaesthesia it is used to neutralize fear when bringing the patient into the operating theatre.

It is a criticism of our technique when it is necessary to neutralize by a potent drug a fear that never should have arisen. Fear comes when facing the decision to

undergo an operation. It arises again as the patient becomes unconscious, and it is for us to see that this latter fear is non-existent. This needs a technique that will cause a patient to enter the operating theatre not as a chamber of horrors, but as a place where he is to receive relief from pain, discomfort or disease, and where he will face calmly a short period of oncoming unconsciousness.

Such a technique is more than mere operative technique. It is a mental technique and it covers more than the time when the patient is in the theatre. There is also the period between the admission to the hospital or nursing home and transmission to the theatre and the period between the decision to undergo operation and the entry to the institution. Without this mental technique surgery under local anaesthesia is impossible. With it the barbiturates and avertin should be unnecessary adjuncts to general anaesthesia.

H. E. G. Boyle : Almost all will agree that basal anaesthesia has been of enormous advantage especially in throat cases, since it removes most of the element of fright before the operation and allows a certain amount of freedom from pain afterwards. The basal anaesthetics that I prefer are nembutal, avertin, and paraldehyde—in that order. Having administered a suitable basal anaesthetic, I give gas-oxygen and ether, only using sufficient ether to enable me to pass a Magill nasal tube into the trachea. When that is in position, the rest of the operation is easily conducted under gas and oxygen alone, or nearly alone. This is a particularly useful type of anaesthesia and has the great advantage of being safe. Should anything untoward occur, one can readily change to carbon dioxide and oxygen, which is the best restorative agent.

With this method suction is essential. When, in 1921, I introduced suction for this type of case I think that my Sorensen pump was the second in this country. Mr. Zamora had one in use about a couple of months before. Next, an adequate gag is necessary, and the Davis gag, introduced by me in 1921, seems to fulfil this.

I was brought up to what used to be known as the "Butlin position", namely with the patient lying on one side with the opposite shoulder slightly raised. This permits all the blood to collect in the dependent cheek and was particularly important in the pre-suction days. Nowadays the surgeon seems to prefer the patient on the back, with the head extended—a good position, but the blood is apt to collect behind the soft palate and may be inhaled; or what is more likely, give rise to middle-ear trouble. When a good deal of blood is likely to collect in the throat, as for example, in the Horgan operation, we use the tube known as Rowbotham's. My difficulty with this tube has been to pass it, for from its shape, it is extremely difficult to see past the bulb and down the laryngoscope. To obviate this I have devised a long catheter which can easily be passed into the larynx, and the large tube can be threaded over the long smaller one. In this way, what was before a formidable performance has now become comparatively simple.

W. S. Thacker Neville : I propose to consider the subject from the point of view of one who has never, until recently, worked with specialists in anaesthesia, and most of whose anaesthetics are given by a recently qualified house surgeon. In 1917, I began to use morphine and scopolamine, followed by local anaesthesia.

After the late war, I went to America, saw that all nasal work there was done under local anaesthesia, and so when I was put in charge of the ear, nose, and throat work in the Missionary Medical College in Mukden, where there were no skilled anaesthetists available, I naturally adopted local anaesthesia preceded by morphine and scopolamine. The advantage of this form of anaesthesia is that it does not require a skilled anaesthetist.

I continued its use for six years in China, and for about four years in England. In 1929 I reported on 150 cases, abstracted out of 461 operated on in Darlington under

morphia and scopolamine and cocaine anæsthesia. The dose was morphine sulphate gr. $\frac{1}{4}$; scopolamine hydrobromide gr. $\frac{1}{100}$; digitalin gr. $\frac{1}{10}$; and after one hour's interval, scopolamine hydrobromide gr. $\frac{1}{100}$; digitalin gr. $\frac{1}{10}$. This was used in 83 cases in which the average weight was 9 st. 3 lb., whilst in 34 cases in which the average weight was 7 st. 2 lb. the second dose was reduced to scopolamine gr. $\frac{1}{200}$, and in 23 cases only the first dose was administered. The second dose was never administered unless the patient was awake and alert one hour after the first dose. The morphia was never repeated. I believe that the largest dosage used was excessive and that the second dose ought to be limited to scopolamine gr. $\frac{1}{200}$.

In three cases lobeline was required on account of shallow breathing, and one patient required strophanthin. The digitalin given with the morphia and scopolamine controlled the pulse.

The immediate mortality of the 461 cases was two, that is, two patients did not recover consciousness. The late mortality was two, that is, one died of pneumonia and the other had phthisis and empyema and died two days after the operation. Children under 14, asthmatics, and stout women over 40, took the anæsthetic badly; for such patients, this form of anæsthesia is contra-indicated.

In 1930 I reported 28 operations under avertin followed by local anæsthesia or ether. At that time Sir StClair Thomson pointed out that the absence of the cough reflex and the long period of unconsciousness made avertin an unsuitable anæsthetic for laryngeal surgery.

The routine in nasal operations is that the patient is given a full dose of avertin and atropine gr. $\frac{1}{75}$ is injected. After thirty minutes, or longer if the patient is not asleep, six cotton-covered probes are dipped into adrenaline and then into pure cocaine hydrochloride, and three are inserted into each nostril to produce block anæsthesia. If an external operation is to be performed, novocain 0.125, potassium sulphate 0.1, normal saline 25 c.c. is injected subcutaneously or submucously. After ten minutes the probes are removed. The patient is now ready for operation or for general anæsthesia.

Ether is given on a mask till the patient is quiet, and marine sponges are inserted into the post-nasal space. Then Flagg's intratracheal tubes are introduced, and the mouth is packed with gauze. The distal ends of Flagg's tubes are shaped like a Jackson bronchoscope, whilst the proximal end is made of spirally wound wire, and is covered with thin rubber. If local anæsthesia is employed, I employ an intra-nasal plug of gauze, as the insertion of a post-nasal sponge disturbs the patient too much.

For tonsillectomies I have used local anæsthesia, with the patient in the recumbent position. With local anæsthesia, the operation can be painlessly performed and its advantage is that blood does not conceal the field of vision. Adrenaline must be sparingly injected, or else secondary hæmorrhage will take place. The post-pharyngeal wall must not be anæsthetized, or the cough reflex will go. More often I use avertin or paraldehyde as a pre-anæsthetic and follow up with ether, given through a Boyle-Davis gag, the patient's head being fully extended. Suction is maintained throughout the operation.

The adenoids are first removed and then the post-nasal space is packed with a gauze sponge with a tape attached. After this the tonsillectomy is performed, all blood-vessels are ligatured, and by the time the operation is completed the hæmorrhage from the adenoid area will have stopped.

The pre-anæsthetic in children differs from that in adults, as children do not like rectal interference and since 1933 I have given children sodium soneryl by mouth. The full dose, according to weight, is administered one hour before the operation, and half an hour later half a dose is administered. For a child weighing 4 or 5 stones, we give two capsules one hour before operation, and if the child is not asleep in half an hour, an extra dose of 1 capsule is given. The powder is removed from the capsule and shaken on to the tongue with sugar. Previous to this belladonna is

given by the mouth. One hour after the first dose of sodium soneryl, the child is anaesthetized.

In guillotine operations, we use 3 c.c. ethyl chloride and 3 c.c. ether in a closed ethyl-chloride bag. If sodium soneryl has been used, ten inspirations of this mixture suffices to produce anaesthesia; if sodium soneryl has not been used it is necessary for the child to take 50 inspirations.

The advantage of this pre-anaesthetic is that if a patient has post-operative hæmorrhage, he can easily be aroused. If he aspirates a blood-clot, the nurse opens the mouth and places her fingers on the back of the tongue, with the result that the child awakens and coughs. Nevertheless, as he sleeps for hours after the operation, we do not give the drug unless he is retained as an in-patient. At times, though seldom, children are restless on recovery, and if so, port wine quickly quiets them.

The last anaesthetic to be considered is evipan. This has been used in short operations such as submucous resection of the nasal septum, removal of aural polypus, and insertion of radium into the mouth. At first it was used alone, but in spite of local anaesthesia the patients became restless, therefore it is now always preceded by omnopon gr. $\frac{1}{2}$ and scopolamine gr. $\frac{1}{300}$. Such a combination gives about twenty minutes of anaesthesia. At times the evipan has been repeated, so that 20 c.c. was used for a radical frontal sinus operation when omnopon and scopolamine were not employed.

The anaesthetic now on trial for nasal cases is pentothal. In two cases omnopon gr. $\frac{1}{2}$ and scopolamine gr. $\frac{1}{300}$, with atropine gr. $\frac{1}{100}$, was used as premedication. One patient, a man aged 25, had a double frontal sinus operation. He went to sleep after 3 c.c. had been injected intravenously, and the breathing, as is usual, was very shallow. The local anaesthetic was injected and then the patient moved, so a further 3 c.c. was injected. The operation was continued and periodically, when the patient moved, from 2 c.c. to 3 c.c. was injected. The operation lasted thirty-five minutes, and 20 c.c., divided into nine doses, was injected. At the end of the operation, 5 c.c. of coramine was injected intravenously and the patient recovered consciousness in two hours and fifty minutes.

In the second case a septum operation was done in twenty-seven minutes, with 14 c.c. of pentothal injected in six doses. Following on this ether was administered with a Boyle-Davis gag for dissection of tonsils. For the first five minutes an ordinary amount of ether was given, and for thirty minutes, the time of the operation, very little ether was required; coramine was injected at the end of the operation.

A. W. Matthew: The danger of foreign material entering the respiratory tract during anaesthesia for nose and throat operations can be avoided in two ways: (1) By occluding the airway by an endotracheal tube and packing, or (2) by maintaining unimpaired the defensive reflexes of swallowing and coughing. While the technique adopted must always be determined by the requirements of the individual operation, the latter method can be used with complete safety in routine nose and throat operations, if the details of the technique have been thoroughly mastered.

There is no doubt that this method is unfashionable at present, and it is difficult to assign a reason. My experience has proved that the plea of danger is untenable. Other reasons must be sought, and perhaps the greatest is the slogan of basal narcosis with gas-and-oxygen; though the freedom from responsibility for the airway at the time of operation, conferred on the anaesthetist by the passage of an endotracheal tube, and the tendency that there is for specialists to specialize without serving an apprenticeship, must play a part.

The long-acting basal narcotics, avertin, nembutal, or morphia, should not be used with this technique, as they all tend to impair the defensive reflexes both at the time of operation and after. This last consideration may well raise the question whether these drugs should ever be used for these operations.

Atropine gr. $\frac{1}{100}$, should always be given forty-five minutes before operation, and my experience to date leads me to believe that a small dose of evipan sodium can be given with safety, as it appears to increase rather than to diminish the reflexes, but anæsthesia should then be induced with ether or gas and ether, chloroform being used with great caution. If evipan sodium is omitted any method of induction may be used, though I favour a chloroform-ether mixture in adults and ethyl chloride or gas in children, the anæsthesia being carried on in both cases by a Shipway's apparatus, chloroform or ether, or both, being used as required. It follows that gas-and-oxygen is not my choice of anæsthetic for these cases, because the use of a pre-operative narcotic is almost essential if the gases are to be used without a liberal admixture of chloroform or ether; endotracheal administration is essential, and I am convinced that gas-and-oxygen increase hæmorrhage.

The introduction of an endotracheal tube is not difficult and seldom causes sufficient injury to inconvenience the patient subsequently. There is no doubt, however, that if the tube is in position for any length of time, the laryngeal and tracheal reflexes become impaired and I am always anxious if the patient does not cough when the tube is withdrawn. The passage of a catheter into the trachea through the nose is more difficult and should always be preceded by an examination of the nose to avoid causing nasal hæmorrhage.

A great deal has been written about anæsthesia for tonsillectomy, especially with regard to the avoidance of psychological trauma in children, and it seems to me that sufficient stress is not laid on the fact that the average child is very sensible and full of confidence in its elders. In these circumstances, if the anæsthetist is tactful and gives the child a truthful explanation of what he is going to do, my experience is that fear of the unknown is replaced by tolerance of the known, and the child does not bear ill-will or resentment afterwards. The unapproachable child is one in whom the natural confidence has been replaced by suspicion, either by broken promises in its daily life or by previous mismanagement of an uncomfortable ordeal, and these are the cases in which preliminary narcotization is justified. Nembutal by mouth and paraldehyde *per rectum*, are the drugs I am in the habit of using in these circumstances, though the depressed respiration and the deep post-operative sleep that sometimes follow their use may cause anxiety.

For tonsillectomy the supine position with the head extended by means of a sandbag placed under the shoulders is the most satisfactory. Anæsthesia, having been induced, is carried on by means of a Shipway's apparatus, and a Junkers' tube or a Davis gag. If a sucker is not used, the post-nasal space should be emptied of clot at the end of the operation by placing a swab in the pharynx and raising the head.

For nasal operations anæsthesia is induced with the patient in the position in which he will remain for the whole operation, and the nasal plugs should not be removed until anæsthesia is established; the anæsthesia is carried on by means of a Shipway's apparatus and a well-fitting airway. Care must be taken to see that the swallowing reflex is not lost, and this can be tested quite easily by suddenly increasing the strength of the vapour, which will always cause the patient to swallow if the reflex is unimpaired.

I do not favour the routine use of a post-nasal plug, but it is the surgeon's prerogative to demand it if he wishes; it is also his prerogative both to insert and to withdraw it, as he is in closer contact with the patient than the anæsthetist is, and has more time to explain why an intra-nasal antrostomy should cause injury to the soft palate. Post-nasal plugs are unreliable and if their use is necessary, endotracheal administration should be considered.

If the word "never" is ever justifiable, I think that its use with regard to preliminary narcotization in operations involving the removal of growths from the pharynx and larynx is one of the occasions. Narcotics of any sort should never

be given before these operations, and premedication should always consist of atropine gr. $\frac{1}{100}$ and nothing else.

I have had the opportunity of anæsthetizing a sufficiently large number of patients for the operations of lateral pharyngotomy, laryngofissure, and partial and total laryngectomy, to have been able to give a fair trial to gas-and-oxygen, chloroform and ether, and the result of my experience is the conviction that chloroform, if well tolerated by the patient, is the anæsthetic of choice for these cases. With chloroform the depth of anæsthesia can be altered rapidly to meet the requirements of the surgeon, the respiration is quiet, salivation and hæmorrhage are reduced to the minimum, post-operative vomiting is the exception, and the quantity of the drug used is very small. If chloroform is not well tolerated I use a chloroform-ether mixture, or even pure ether, but I have given up using gas-and-oxygen.

It is a great advantage for the preliminary tracheotomy that accompanies these operations to be done under local anæsthesia.

D. F. A. Neilson: I propose first to give a few reasons why I look upon general anæsthesia as more beneficial to the individual patient than local anæsthesia, without reference to the patient's mental or bodily comfort, or to the matter of expense.

The commonest, and one of the easiest, operations to perform under local or general anæsthesia is tonsillectomy, and it has the advantage, for comparative purposes, that when carried out under local anæsthesia the administration of morphine and its derivatives rather hinders than helps, and therefore is contra-indicated.

The points to be considered are:—

(1) Under which anæsthetic the operation can be most skilfully and rapidly carried out.

(2) Under which the patient runs the least risk of reactionary or secondary hæmorrhage.

(3) Under which is the greater risk of lower respiratory infection.

(4) Which leads to the most speedy recovery.

When the operation is performed under general anæsthesia the use of the Davis gag has made the removal of the tonsils a comparatively easy performance. The head being fully retracted and a nasal tube conducting the anæsthetic directly into the trachea, there is no danger of the air-way becoming obstructed.

Removal of every type of tonsil under local anæsthesia requires much greater surgical skill.

Reactionary hæmorrhage is the most dangerous complication of tonsillectomy, and, provided sufficient time can be sacrificed to any given case when a basal narcotic is used, it is possible to remove the endotracheal anæsthetic tube with the Davis gag still in position, and to keep watch on the operation field after the end of the operation itself. The basal anæsthetic will be sufficient in most cases to keep the patient quiet enough for any bleeding point to be secured.

In the extended head position there is no danger of the lower respiratory tract becoming invaded by blood or septic fluid during the operation. There is perhaps some risk of this after the operation unless measures are taken to see that the position of the patient is satisfactory while he is still unconscious under the basal narcotic.

When tonsils are removed under local anæsthesia the patient is usually in the upright position. There must be a slight risk of blood getting into the tracheal passages during or immediately after the operation, especially if there is any unexpected hæmorrhage which may cause coughing and temporary spasm. Patients whose tonsils have been removed under local anæsthesia undoubtedly eat and are able to get about more quickly than is usual after a general anæsthetic, and for this reason they are able to get back to normal life one or two days earlier, but

there must be just as much risk of secondary hæmorrhage occurring during the later days, whether the anaesthesia has been local or general, and there is more danger of hæmorrhage immediately after the operation when a local anaesthetic is used.

I do not see any objection to opening a peritonsillar abscess, or any abscess deep to the pharyngeal wall, under a general anaesthetic, provided the patient is in the same position as for removal of tonsils with the Davis gag. The abscess wall can be incised and a good drainage opening obtained without the agonizing pain which patients sometimes have to suffer. The pus and blood can be aspirated and the patient retained for some minutes under observation until all oozing has ceased. I consider it extremely dangerous to attempt to evacuate pus from the pharynx under a short or light general anaesthetic. Spasm of the larynx may occur, and a deep inspiration will suddenly be taken, and it is possible under these circumstances for anything in the mouth or pharynx to be sucked into the trachea.

Apart from the scientific aspect of the question, I am sure that in this country the vast majority of patients are in favour of operations under general anaesthesia in preference to local anaesthesia. This must be due in large measure to their confidence in the skill of the anaesthetists, and I venture to think that where local anaesthetics are extensively used, it is because expert general anaesthetic administration is not available. I have noticed myself during the last eight years and have been told by surgeons themselves who favoured the use of local anaesthetics, that they have been forced either by temperamental stress or by the complaints and observations of their patients, to give up the use of local anaesthetics and revert to general anaesthetic methods.

J. H. T. Challis: I propose to touch on the questions of premedication and the administration of pure gas-and-oxygen in operations on the upper air passages. First I will sum up the position from the patient's point of view. He demands to know whether he is to be put to sleep in his bed, as he has heard that this is the nicest way. Should you inform him that this type of anaesthesia is unsuitable for the particular operation that is being performed, you will immediately be told that he knows somebody, or has heard of somebody, who has had it done that way. To this there is no answer. Therefore, I am afraid that wherever possible I take the line of least resistance and administer the anaesthetic of the patient's choice. But I have grave doubts whether I am being fair to myself or my patient. To sum up these doubts: (1) The addition of one single unnecessary drug, however innocuous in itself, shows lack of skill. (2) Should that drug be known to be dangerous, or to have ever proved fatal, or to have increased the period of normal convalescence, I cannot but think that its use is to be deprecated.

I suggest that as far as our present knowledge of anaesthesia goes, the ideal is omnopon and scopolamine, followed by gas-oxygen and ether, sufficient ether only being administered to allow the easy passage of an intratracheal tube, maintain a quiet and even anaesthesia, and eliminate all possible symptoms of anoxæmia. There is one definite exception to the foregoing procedure, and that is in major operations on the larynx. Here we are almost always dealing with old people whose general condition is poor. So far I have 100% mortality with the administration of heavy premedication, but since adopting the technique of atropine, followed by intratracheal gas-oxygen, and the minimum of chloroform, and post-operatively only such mild narcotics as bromide and aspirin, the mortality has been sufficiently low to make this operation very well worth while. So far I have found that the administration of pure gas-and-oxygen, unless the occasion demands it, for operations on the throat, nose, or mastoid process, is not justified, as patients tend to bleed and ooze more, and vessels are more difficult to pick up, thereby prolonging the time of operation and fraying the temper of the surgeon in his endeavour to perform an intricate operation at the bottom of an inkpot.

In conclusion I should like to put forward two suggestions for discussion :—

(1) Has not the pendulum in favour of heavy premedication swung too far for the safety and well-being of the average patient ?

(2) Is not the administration of pure gas-and-oxygen rather a disadvantage than an advantage to the surgeon ?

Z. Mennell said that he frequently saw hæmorrhage from a tonsil bed kept up by a constant stroking and removal of a clot by a violent sucker. A sucker, though useful, could be very much abused. That there should be co-operation between the anæsthetist and the surgeon he never had any doubt. There were certain cases, for instance cases of tonsils and adenoids in children, in which the psychological element was not sufficiently considered. It was a dreadful thing to give a child an anæsthetic without premedication. Of that premedication, especially for children, there was nothing so safe as the old-fashioned paraldehyde.

He had been glad to hear more than one speaker mention chloroform. Reference to chloroform at a meeting of anæsthetists was, nowadays, almost barred, but he had always felt that a very strong case was to be made out for chloroform for certain operations about the nose and throat. A point which had not been brought out was the danger of using chloroform after a local anæsthetic in a case in which a hæmostatic had been used, the latter, almost always, being adrenaline. Though he had not seen it, it had been proved in experiments on animals, that a mixture of chloroform and adrenaline would cause ventricular fibrillation. That was a fact which probably most of those present knew, but he had received a paper from his friend Wesley Bourne, of Montreal, in which the same condition was described as occurring, at all events in animals, after the use of avertin and adrenaline.

C. A. Scott Ridout said he was very glad to hear it said that of all the anæsthetics, to one who knew how to give it, chloroform was the simplest. He considered that paraldehyde, in children, as a basal anæsthetic, chloroform and ether mixture, skilfully given, and gas-and-oxygen, were the three anæsthetics of choice.

I. W. Magill said that he was surprised at the lack of support for local anæsthesia for tonsillectomy in adults. He had been most favourably impressed with this method at the Mayo Clinic.

Oozing from the tonsillar fossa was sometimes increased by excessive extension of the head, and by forcible use of a Davis gag. Both factors tended to impede venous return. To appreciate the congestion, even without the addition of the gag, it was only necessary to lie conscious on a table, with the head thus extended by means of a sandbag behind the shoulders. Further, this position did not protect the larynx from the entry of blood so effectively as it was popularly supposed to do. It had been demonstrated that blood could be drawn into the larynx on inspiration, against the force of gravity.

Harold Sington said that with the use of paraldehyde there was likely to be rowdiness on the part of the patient if it was rapidly introduced *per rectum*. In the use of that drug, the more slowly it was given, the less likely was the patient to be restless afterwards ; in this respect it was analogous to alcohol.

One speaker had objected to premedication because it was so long before the patient came round. With children that was a great advantage. Children who had had a dose of paraldehyde had no pain the next day, and were comfortable, and took their food as usual.

Another interesting point concerned the dose of atropine. Generally, too small a quantity was used. He gave big doses of atropine to children under 10 years of age and from $\frac{1}{75}$ to $\frac{1}{50}$ gr., from 10 to 12 ; in winter, when many children had colds, he increased the dose. It seemed to abolish all moisture in the bronchi. If big doses of atropine were used, bronchopneumonia did not occur.

Clinical Section

President—B. T. PARSONS-SMITH, M.D.

[April 9, 1937]

Diffuse Sclerosis.—NEILL HOBHOUSE, M.D.

Peter B., aged 9½ years. Parents healthy; two younger children normal. He seems to have been a normal boy in every way until about June 1936. He suffered from some febrile attack in which he was drowsy, but was able to return to school a week later. After this, as is shown by his exercise books, mental deterioration steadily progressed.

25.11.36: He was admitted to the West End Hospital. He was quiet and fairly well behaved, but inclined to wander about aimlessly. He talked a little and could give his name and address. There was no defect of hearing, and he would obey an order which was repeated several times. Vision could not be tested, but seemed fairly good. Gait was stiff and awkward. Muscle tone was not appreciably altered. Deep reflexes were brisk; abdominals very variable; plantars usually flexor left, extensor right. Cerebrospinal fluid was normal except for 0.06% protein.

The mental deterioration continued since admission; now he is completely demented and very dirty in habits. Rapid failure of vision was noticed in January; he is now almost blind.

Condition on 31.3.37: Pupils dilated and react sluggishly. Arms: tone slightly raised in the right; occasional groping movements. Abdominal reflexes not obtained. Increase of tone in the right leg. Deep reflexes brisk, plantars extensor right, doubtful extensor left. Report on fundus (Mr. Sorsby): Since December 1936 the discs have been getting more white. That a progressive atrophy is taking place cannot be questioned.

The combination of progressive intellectual deterioration, failure of vision, and disturbance of the pyramidal tracts, with no indication of raised intracranial pressure, suggests some demyelinating condition of the nature of diffuse sclerosis or Schilder's disease.

Solitary Plasma-celled Myeloma of the Vertebral Body, causing Paraplegia.—A. DICKSON WRIGHT, M.S.

Kenneth A. H., aged 31.

In April 1936, the patient noticed progressive weakness in walking. Six weeks after the onset he could not walk at all, and there was absence of sensation from the 11th dorsal nerve downwards. A skiagram taken at this time showed destruction of the 8th dorsal vertebra, due either to tuberculosis or neoplasm.

Operation (June 13, 1936): the laminae of the 6–10 dorsal vertebrae were removed, and it was noticed that the spinal theca was flattened from the pressure of the growth in front; the dura was not opened, but was retracted to one side, when the body of the 8th dorsal vertebra was found to be replaced by a pulsating growth. The growth was opened and removed with a sharp spoon. The hæmorrhage, which was profuse, was arrested by packing and the wound closed. The patient was nursed on a plaster bed.

Costo-transversectomy July 17, 1936: The body of the 8th vertebra was exposed from the right side and twenty radon seeds ($\times 2$ millicuries) were inserted in the growth. The patient made a good recovery from this operation except for the development of a left femoral thrombosis. Two months after the operation a severe hæmaturia occurred. This was investigated and, no cause being found, it was attributed to an infarct.

Pathologist's report on portion removed at first operation: Plasma-celled myeloma.

After two months in bed the patient was allowed up in a steel brace. He has improved steadily, and at the present time is practically normal.

JUNE—CLIN. 1

Discussion.—Dr. PARKES WEBER said that, had Bence-Jones protein been detected in the urine, he would have regarded the case as an example of the commencement of progressive (fatal) myelomatosis. In the present patient there was no evidence of atypical amyloidosis, which was present in a considerable proportion of myelomatosis cases—a connexion of extreme pathological interest.

Mr. DICKSON WRIGHT (in reply) said he understood the purport of Dr. Parkes Weber's remarks to be a query whether the appearance of Bence-Jones proteose with a solitary plasma-celled myeloma meant inevitable dissemination and death of the individual. There were in the literature undoubted cases of solitary myeloma, in which the proteose had been present but had disappeared after complete removal of the growth, and the patients had survived without recurrence. In the vertebral column the prognosis was different because of the impossibility of eradicating the disease in the way possible in the limbs. There were four cases of solitary myeloma of vertebra in the literature, and post-mortems in three cases showed the disease to be confined to the one site. In the case presented to-day, complete skiagrams had shown no deposits in other bones, and no Bence-Jones proteose had been found in the urine.

Felty's Syndrome (Chauffard-Still Syndrome).—F. PARKES WEBER, M.D., and A. SCHLÜTER, M.D.

"Felty's syndrome" is a convenient term for the combination of symptoms of chronic or subacute rheumatoid arthritis in an adult, with enlargement of superficial lymphatic glands and spleen. Though the exact causation of this syndrome is not known, it is probably of chronic infectious nature and analogous to "Still's disease" in children. Just as in the latter, enlargement of the spleen is sometimes not obvious, so in Felty's syndrome the spleen may not be palpable.

The patient, W. L. C., aged 24, a thin, dark-complexioned young Englishman, was first seen by us in January 1937. He had enjoyed ordinary health until about May 1935, when the present illness commenced with painful swelling of the left wrist-joint, which temporarily diminished, but did not leave him. For the last four weeks he had had painful swelling in the right wrist and more recently a variable painless swelling in the right finger-joints. Slight pain in the knees, without swelling or stiffness, was complained of. There was moderate, painless, soft, discrete swelling of the lymphatic glands in both axillæ, and the supracondylar and inguinal glands were also slightly enlarged on both sides. A freely movable subcutaneous nodule, of the size of a large olive, on the inner side of the left upper arm, about four fingerbreadths above the elbow, was afterwards excised for "biopsy" purposes and was found on microscopical examination to be a hyperplastic lymph-gland containing large germinal centres of Fleming; no evidence of tuberculosis. Teeth and gums: unsatisfactory.

By ordinary examination of the thorax and abdomen, and by X-ray examination of the thorax, nothing abnormal was found; the spleen and liver could not be felt, though by percussion the spleen seemed to be somewhat enlarged. Radiograms of both wrist-joints showed atrophic arthritic changes. In February it was found that the right elbow-joint had also become swollen, somewhat hot, but only slightly painful. The erythrocyte-sedimentation rate, taken several times in December, January and February was always found to be accelerated; on February 2 it was twenty-eight minutes and on February 10 it was thirty-five minutes (normal is over an hour by the method employed). The blood-count showed slight anæmia. Blood-Wassermann reaction negative. Blood-serum calcium: 11 mgm. per cent. The urine showed nothing abnormal. Brachial blood-pressure: 130/95 mm. Hg.

The patient's father, who died from abdominal cancer at 59 years, is said to have suffered badly from rheumatism.

POSTSCRIPT.—At the meeting the spleen could be felt quite definitely enlarged. Pirquet cuti-reaction: Negative (April 10). Body-weight: 52.1 kilograms (in clothes). Said always to have been thin. Blood-count (April 13): Hæmoglobin 88%; erythrocytes 4,460,000; leucocytes 7,200. Erythrocyte-sedimentation rate (April 13): thirty-seven minutes.

Dr. PARKES WEBER said he thought that "Felty's Disease" was probably really the same as Still's disease in children. If so, the disease might occur at any age from infancy to adult life. He had seen it in a boy in whom it had commenced about 1892, at Harrow school, or earlier. This boy recovered and became a medical doctor, but had several recurrent attacks, in one of which he developed pericarditis, as in some of Still's cases. He might, however, have had true acute rheumatism as well as Still's disease. At the present time, at the age of 60 years, he looked well and was fairly active, but had auricular fibrillation and had constantly to take a digitalis preparation.

He (Dr. Weber) hoped that gradual recovery would occur in the present patient, without the help of gold treatment, which was dangerous. The teeth and gums needed special attention, but the pulling out of many teeth at a time in such a chronic infectious condition was certainly dangerous.

The Nonne-Milroy-Meige Œdema, of late onset, in Sisters.—F. PARKES WEBER, M.D., and A. SCHLÜTER, M.D.

Mrs. F. A., aged 32, English. Chronic œdema of the feet and legs up to the knees, developed gradually at about 22 years of age. At first it disappeared with a night's rest in bed, but later it took several days in bed to effect complete disappearance. No disease of thoracic or abdominal viscera. Blood-count: Hæmoglobin 80%; erythrocytes 4,140,000; leucocytes 5,500. Brachial blood-pressure: 140/80 mm. Hg. Urine: Nothing abnormal. Negative Wassermann reaction. The patient suffered from epileptic fits up to puberty, and of her four children, one (a boy aged 2½ years) is mentally backward.

Gertrude S., aged 30 years, sister of the above, has enjoyed ordinary health, except for chronic œdema, and tendency to ulceration of both legs. The œdema commenced gradually about the age of 20 years. Brachial blood-pressure: 122/75 mm. Hg. Blood-count: Hæmoglobin 85%; erythrocytes 4,340,000; leucocytes 8,600. No heart disease. Rather fat and coarsely built. Never epilepsy.

A third sister, Mrs. A. M. S., aged 28 years, is said to be thin and to enjoy good health, but at about the age of 20 years œdema of both legs gradually developed. No leg ulcers. Never epilepsy.

A fourth sister, Mrs. E. F., aged 38 years, is said to have gradually developed œdema of both legs at about the age of 20 years. Has suffered from ulceration of one leg. Never epilepsy.

These four sisters have other brothers and sisters, said not to be affected with leg œdema. No other family history obtained.

In our experience, œdema of this kind in one or both legs, commencing at about 20 years of age, occurs mostly in females, and without history of a similar condition in other members of the family.

Discussion.—Dr. PARSONS-SMITH commented on the uncertainty in regard to the actual pathological basis of the Nonne-Milroy-Meige and other rare forms of œdema; he suggested that estimation of the venous pressure might be of value in such cases, also investigations regarding the questions of the permeability value of the vessels and the protein content of the blood plasma.

Dr. W. F. HAMILTON asked Dr. Parkes Weber whether he had seen this type of œdema associated with defective enamel of the teeth.

Dr. PARKES WEBER (in reply) said that a name was necessary to distinguish this class of œdema from other classes. Nonne, Milroy and Meige all deserved credit for directing attention to the subject. There were many isolated examples in which no hereditary or familial history of a similar condition could be obtained. If one termed these cases hereditary or familial œdema, a general practitioner might say that his case must belong to some other class, as it was neither hereditary nor familial. He might then proceed to try cardiac drugs and all manner of useless treatment. He might try a course of rest in bed, with massage of the legs, leading to temporary disappearance of the œdema. But the œdema returned on the patient's getting up, and no useful purpose was served. Bandaging should be used to prevent the œdema from becoming excessive. In extreme cases rest in bed might be required

for a time. Above all, however, general practitioners should learn to recognize this class of cases, and thereby spare themselves and the patients much trouble. Differential diagnosis would never be obtained if the cases were termed merely hereditary or familial oedema.

Apparently no abnormalities in the enamel of the teeth had been noted in these cases.

The President's suggestions for clinical investigation would probably be difficult to carry out. Expert histological examination might ultimately throw light on the condition, but when patients died of some totally different disease, the old chronic oedema was not likely to be thought of; indeed, the oedema was not likely to be very noticeable when the patient died after a long illness in bed.

Seven Cases of Carcinoma showing Result of Treatment.—DUNCAN
C. L. FITZWILLIAMS, C.M.G., F.R.C.S.

I.—Mrs. W., aged 53. Admitted to St. Mary's Hospital, April 1932.

History.—Noticed swelling in left breast, lower and outer quadrant, for two months.

April 15, 1932: Local excision of tumour; some glands removed from axilla. Breast replaced by a lipoma removed from the patient's side. An interstitial dose of radium, 432 mgm.-hours, was given to the axilla.

Pathologist's report.—Carcinoma.

October 28, 1932: Surface radiation to breast, 10,640 mgm.-hours.

February 7, 1933: Supraclavicular gland thought to be suspicious.

January 18, 1937: Telephoned to say she could not attend but was quite well.

II.—Mrs. G., aged 46.

Admitted to St. Mary's Hospital, December 1931.

History.—Noticed swelling in left breast seven months previously, beginning to be attached to skin; free otherwise; 1.5 × 1 cm. in size. No glands felt in the axilla. Glands could be felt in the neck but were not considered carcinomatous. Shadow on transillumination.

Local removal of part of breast, containing tumour; nothing else disturbed.

Pathologist's report.—Carcinoma with numerous mitotic figures.

February 2, 1932: Transferred to Mount Vernon Hospital for radium treatment. Had surface radiation and was given a total dose of 40,000 mgm.-hours, 28,000 to the breast and 12,000 to the axilla. Has been under observation since and is perfectly well.

III.—Miss E. P., aged 61. Admitted to St. Mary's Hospital, September 20, 1934.

History.—Blow to left breast five weeks ago. A week later noticed a lump in the breast, but has had no pain.

There is a hard rounded lump in the outer part of the left breast, the size of a small walnut; not attached to the skin. Secondary glands in axilla.

September 25, 1934: Local excision of part of breast. 4,008 mgm.-hours of radium.

Pathological report.—Carcinoma.

June 8, 1935: Readmitted for treatment by plaque. 15,300 mgm.-hours given. Desquamation followed. Well ever since.

This case was not considered suitable for local excision as it did not conform to my definition of an early case, but the patient's wishes had to be considered.

IV.—Mrs. E. G., aged 66. 22.7.33: Admitted to St. Mary's Hospital.

History.—Tumour known to be in the breast for nine months. Not attached to skin; size of a broad bean; hard, defined. No glands felt in axilla.

Operation (24.7.33).—Local excision. Some glands removed from axilla and radium inserted; 3,168 mgm.-hrs. to remainder of breast.

5.9.33: Fibrosis of remainder of breast took place and has remained ever since.

Pathological report.—Solid alveolar and trabecular polygonal-celled medullary

carcinoma, with metastases in axillary glands. Cells variable in size and shape, mitotic figures frequent.

23.12.33 : Surface radiation, 5,040 mgm.-hours to breast and 11,160 to axilla.

4.5.36 : Surface radiation again given as a precautionary measure in view of the pathological report.

Perfectly well to date.

V.—Mrs. A., aged 59. Admitted to St. Mary's Hospital December 2, 1932.

History.—Swelling in left breast noticed five months ago; increased in size very rapidly of late. No discharge from the nipple. The swelling was hard with a definite edge and was the size of a tangerine orange. It was in the upper and inner quadrant of the breast, not attached to the skin or deep tissues, but casting a deep shadow on transillumination. A hypodermic needle was inserted and some dark yellow opaque fluid was drawn off.

The tumour was excised locally through a circum-areolar incision.

Pathological report.—A fibrosarcoma originating in a previously existing fibroadenoma.

Patient transferred to Mount Vernon Hospital in February 1933 and surface radiation given; 25,440 mgm.-hours to the breast, 8,640 to the axilla and 13,440 to the supraclavicular area.

Result.—Perfectly well to date.

VI.—Mr. C. V., aged 53.

Admitted to St. Mary's Hospital, May 22, 1931, with an ulcer $\frac{3}{4}$ in. long by $\frac{1}{2}$ in. wide, in the angle between the lower lip and the jaw, near the mid-line. This had been known to be present for seven to eight weeks, and was getting larger. No glands could be felt.

835 mgm.-hours of interstitial radium, 0.5 screenage, was given over seven days. The ulcer healed, but the dose was too small and the ulcer returned. As there was a doubt as to whether there was a radium necrosis or a recurrence, the ulcer was excised, and biopsy showed small islands of active carcinomatous cells. November 18, 1932, 19.5 mgm. of radium was applied to the outer side of the lip till it desquamated freely. In January 1933 the ulcer returned, and was again excised. This time it proved to be inflammatory and not malignant. Since then it has healed and broken down slightly several times, but has never appeared malignant.

VII.—Mr. C. H., aged 66.

Admitted to St. Mary's Hospital, October 19, 1932, with a nodule, between the sizes of a sixpence and a shilling, about the middle of the left border of the tongue. No glands felt.

Treatment.—Interstitial radium, 888 mgm.-hours. The nodule disappeared.

January 13, 1933 : A lump began to reappear and a recurrence was feared.

March 1933 : The tumour ulcerated and was excised. According to the pathological report it was non-malignant, so was probably a radium necrosis. The tongue healed.

In May there were suspicious glands in the neck, and a block dissection was performed. All the glands removed were examined; nothing malignant was found.

March 2, 1937 : A swelling appeared on the back of the neck and was diagnosed as a lipoma; it was removed and this diagnosis was found to be correct. The patient is now very well.

Two Cases of Tuberculosis treated with Tuberculin.—W. CAMAC WILKINSON, M.D., F.R.C.P.

I.—Harold N., aged 33. Married. Two children. No family history of tuberculosis.

Past history.—He had been a helpless cripple for three years. Chronic disease of the spine with stiffening, especially in the cervical region. Stiffening of temporo-maxillary joints; could only open his mouth $\frac{1}{2}$ cm. and had to be fed by a tube. Grating could be felt on movement of jaws. Severe painful stiffening of joints of legs.

Arthritic atrophy of muscles of joints involved. Muscles of chest also affected. In addition to the sloping gait there was a characteristic change in the shape of the chest—like that of phthisis but with characteristic differences.

Sent by Tuberculosis Officer to Brompton Hospital early in 1930. No diagnosis made after three months.

Sent to Paddington Infirmary. Fluid withdrawn from swollen knee and injected into guinea-pig. Result negative. Diagnosis: chronic rheumatism.

I then saw the patient, who was admitted to Maida Vale Hospital, where I tested him with tuberculin. Local and general reactions to all tests. Patient was then treated at home for one year and three months with T.A.F. up to a dose of 1.5 c.c. He reacted constantly, and at times severely, in the affected joints, proving the nature of the joint troubles.

Treated for thirteen months with tuberculin alone. Weight increased from 7 st. 2 lb. to 8 st. 4 lb. After treatment he was able to walk quite well. Could open his mouth $\frac{3}{4}$ in. or more.

January 1932: Walking better. Appetite better. Could open mouth. Movements in neck easier. Returned to work on January 15.

June 1933: Working from 8 a.m. to 5.30 p.m., making aircraft instruments. Able to walk to and from work. Still some restriction of movement in neck.

April 6, 1936: Extract from letter: "Now four years and three months since I restarted work, and I have not lost a day since through illness."

II.—Mr. E., aged 36. Motor driver. Weight 9 st. 13½ lb.

Vague trouble, chiefly with fields of vision, since Christmas, 1932. Headaches in the morning. No vomiting. Operation proposed at hospital.

Patient then seen by me. X-ray examination revealed destruction of bone in sella turcica, indicating pressure of tumour. I then tested for tuberculoma in order to exclude tuberculosis as cause.

August 4, 1933: Reaction to first test dose (0.00025 c.c. T.A.F.) 101° F.

August 11: Reaction to second dose (0.00005 c.c. T.A.F.) 100.6° F. Both also gave very severe track reactions. Also pain on closing and opening eyes. Photophobia and sight worse after the dose.

Steady increase in weight; gained 4 lb. in two months. Tuberculin treatment continued gradually. October 20: Weight 10 st. 8 lb.

March 6, 1934: Eyes improved. Recession of films and lighter films.

March 29: Reached dose of 1.75 c.c. T.A.F. Weight 10 st. 3½ lb. No rise in temperature, after this dose. Both eyes improved. Recession of films and lighter films.

April 23: 0.15 c.c. B.E. Symptoms three hours after dose. Shivering, aching in jaws. Pain definitely behind base of nose, extending to both sides over brow. No doubt, intravenous injection.

May 2-29: Aching of head and blurring of sight after injections.

May 30: 0.55 c.c. B.E. caused temperature of 101.2° F. After reaction was spent, field of vision was wider for some time.

Doses of B.E. continued to 1.35 c.c. B.E. After this dose temperature only 99.2° F. Pause from July 13 to December 27, 1934.

December 27, 1934: Fresh course of T.A.F. March 1935, eyes were specially clear.

June 1935: B.E. was given up to 1 c.c.; reaction to 100.4° F., headache and focal reactions, loss of weight.

Absent in India.

May 1936: Weight 10 st. 6½ lb. Further doses of T.A.F. and B.E.

November 1936: Slight improvement. Can come to Clinic by himself.

March 1937: 2.5 c.c. B.E. Focal reaction, but sight better. Weight now 10 st. 7 lb.

Section of Anæsthetics.

President—C. LANGTON HEWER, M.B.

[March 5, 1937]

DISCUSSION: IMPRESSIONS OF ANÆSTHESIA IN U.S.A. AND CANADA

Mr. R. R. Macintosh, after referring to the hospitality and consideration shown to visiting anæsthetists by their American colleagues, said: In America the appointment equivalent to our resident anæsthetist does not exist. Some years ago the newly qualified house-officer used to spend his first three months giving anæsthetics before moving on to his next job. The surgeon suffered continuously. At the end of three months his anæsthetist, just beginning to master the more elementary difficulties of anæsthesia, would be replaced by a new graduate. The training of nurse-anæsthetists partially solved their problem.

The employment of nurse-anæsthetists does not meet with the approval of the medical profession as a whole, nor with that of the Society of Anæsthetists in particular. The majority of these nurses are selected women from the start. Most of them are well-trained and competent, often having many years' experience behind them, and they are infinitely better anæsthetists than are doctors who give anæsthetics only occasionally. They are not allowed to pass intratracheal tubes, or to give intrathecal or intravenous injections. The difficulty which faces the Society of Anæsthetists is that if by any move of theirs the nurse-anæsthetist is banished, there is not nearly a sufficient number of medical men experienced in anæsthesia to do their work. Replacement of the nurse-anæsthetist must be gradual, or there will again inevitably be a period during which both patients and surgeons will suffer. In the meantime the rewards of the speciality are not enough to attract a sufficient number of medical graduates.

What is the truth about the nitrous-oxide controversy? My feeling is that, in Toledo, gas-and-oxygen anæsthesia is overdone, whilst elsewhere, including this country, it is not practised nearly enough. The cases I saw at Toledo were excellent. Induction and recovery were infinitely more pleasant for the patient than if ether only had been used. The operative conditions for abdominal work were, in the hands of these two experts, what I would describe as "fair," taking London as a standard. There was no straining but there was a tone about the abdominal wall which would certainly bring a look of reproach to the faces of my surgeons. The local surgeons prefer to put up with some operative difficulty in order to achieve freedom from post-operative complications. My own chief post-operative concern is vomiting, and if my patients woke up with as many smiles and as little vomiting as the Toledo patients I should experience less disappointment from anæsthesia.

Secondary saturation, on which success in many cases depends, is not a pleasant sight. On the other hand, if you are not prepared to resort to it when necessary,

you will have failures. I have seen Clement deliberately reduce a patient to respiratory arrest, and then inflate the lungs with oxygen, with excellent subsequent results. As he somewhat lightheartedly says, "When giving pure gas, the second-to-last breath which the patient would take should contain plenty of oxygen." I inquired of him what happened to the blood-pressure in cases of extreme cyanosis. His reply was that the only change of any importance was that the surgeon's went up! I have seen respiratory arrest deliberately induced with open ether, and I saw Rowbotham reach this stage recently during a masterly display of cyclopropane at the Cancer Hospital. We have to face the fact that in all these cases the patients are near death, that in the hands of the man who knows what he is doing the procedure is possibly safe, and that though the "secondarily saturated" patient is the least pleasant to look at from a cosmetic point of view, the expert can bring this patient back to consciousness more quickly and with fewer after-effects than in the case of patients profoundly anesthetized by the more toxic agents.

For most extra-abdominal work the degree of secondary saturation attained is not so severe as I have indicated, but in many cases a degree of cyanosis persists throughout the operation. It is round the colour question that argument generally centres. No one denies that cyanosis is bad for a patient, but so too are chloroform and ether. For an operation to be done a patient has to be rendered unconscious and flaccid by some noxious process. Should he be reduced to this state by a poison such as ether, or should he be given nitrous oxide, which acts largely by oxygen replacement?

Pink anaesthesia is a tradition in this country. In the days of chloroform and ether a blue colour meant respiratory obstruction. The surgeon soon correctly associated alarm and increased bleeding with this condition. The surgeon's reflex has become conditioned, and he still experiences the same fears and makes the same complaint of increased bleeding whenever he sees a blue patient, even though both fears and complaint are groundless. The pathology of the "blueness" in nitrous oxide anaesthesia is due to replacement of some of the oxygen in the blood-stream by nitrous oxide, and exists in the absence of respiratory obstruction which is the cause of the increased bleeding which in turn gives the surgeon justifiable cause for complaint.

The Toledo experts maintain that colour is no guide to anaesthesia. The first patient they gave me to anaesthetize was a negro boy for appendicectomy. I confess to a feeling of insecurity when I embarked on this with no agents other than gas-and-oxygen in the theatre, but with McCarthy's help I managed reasonably well. In other cases I saw him cover the head of the patient with a towel so that a student could learn the signs of respiration, and not be guided at all by colour.

Anaesthetists I met in other cities did not approve of the Toledo technique. Research workers point out that electrocardiograms prove the patient to be in a parlous condition during gas-and-oxygen anaesthesia. Clement counters by saying that whatever the electrocardiogram registers, the patients go on satisfactorily in his hands.

One final impression. I think certain schools in America make the same mistake that certainly I, and possibly many others of us make—they tend to confine themselves to the use of one or two particular anaesthetics. I am told that in Chicago, the home of ethylene, this gas is used as a routine in the hospitals. Some cities use practically nothing else but cyclopropane for major work. The McKesson school persists with nitrous oxide. Each exponent acquires great skill in his own particular method, but if he tries a new one he is liable to have a failure. He is then inclined to blame the new drug and not his own lack of practice in using it. As a confirmation of this I would quote a letter from Toledo, dated January of this year, in which it is stated that they have been trying cyclopropane, but in many cases they have had to switch over to nitrous oxide in order to obtain satisfactory operating conditions.

Dr. H. W. Featherstone (*Abbreviated*): When we visited America and Canada in 1930, my colleagues—Dr. Apperly, Dr. Magill, and Dr. Parsons—and myself, were impressed by these facts:—

(1) Ethylene was employed on a large scale in the United States, but was not in general use in Canada.

(2) The best type of machine for gas-oxygen, and ethylene-oxygen was not generally agreed upon. I think the Heidbrink was most favoured at the Mayo Clinic, the Foregger-Gwathmey gas-metric machine in Montreal, and the McKesson elsewhere. But it was usual to see all the well-known models standing side by side in the theatre anteroom, so that the room looked like a garage or a fire station.

(3) Chloroform was not seen in use; ether was usually employed by the anaesthetic nurses and by the internes.

(4) Before operation atropine was rarely used; morphia and scopolamine were used often.

(5) Spinal analgesia was produced by withdrawing 8-10 c.c. of cerebrospinal fluid, dissolving a measured quantity of sterile novocain crystals in the fluid and then re-injecting the solution into the intrathecal space.

(6) Abdominal relaxation was not called for so insistently as in this country, and when required it was obtained by synergistic methods or by spinal or local analgesia.

(7) The new and powerful barbiturates were coming into general use and the leading clinics were engaged in assessing their value.

(8) Nurse-anaesthetists were seen in most clinics, either working alone with ether on the simpler cases or, under supervision, administering one of the gaseous anaesthetics from a large machine, for more serious operations.

At the time of our visit to the Mayo Clinic, ethylene-oxygen-ether, preceded by a barbiturate, was the favourite major anaesthetic, but I rather gather that nowadays avertin, pentothal, intratracheal methods, and cyclopropane in special cases, are more usual.

Dr. Lundy, the Chief Anaesthetist, was a warm supporter of the principle of supervision. He had nurse-anaesthetists in two or three theatres. He went from one to the other, decided upon the method to be employed, took the main steps (such as giving a barbiturate, or a spinal anaesthetic) and then handed the patient over to the nurse-anaesthetist, who gave ethylene-oxygen and took blood-pressure readings. At that time there were about 1,800 beds in occupation, and only three qualified and trained staff anaesthetists, so that one can realize how large a part the nurse-anaesthetists were taking. I understand, however, that trained and qualified anaesthetists are now replacing nurses.

In the Winnipeg General Hospital in 1930 the senior anaesthetist was on a whole-time salary; working from 8 a.m., he usually finished about 1 o'clock. He had the remainder of the day free. The other anaesthetists received some payment for hospital sessions, fees from private ward cases, and outside anaesthetics, and in addition they did some general practice. At the Montreal General Hospital in the working-class quarter, the chief anaesthetist was on duty from 8.30 a.m. until the routine lists were finished. He was assisted by two resident anaesthetists and an experienced nurse-anaesthetist. He anaesthetized in those cases which he considered to be of special interest or importance, regardless of which surgeon was operating or of whether they were private cases or otherwise. As the anaesthetists were all on a salaried basis, the private ward anaesthetic fees were paid into the hospital anaesthetic fund. The salaries and other expenses of the Anaesthetic Department were paid out of that fund, supplemented if necessary by the hospital main funds.

In Toronto the arrangements appeared to be similar to ours—a staff of visiting anaesthetists who had private practices.

In America and in Canada people expect to enter institutions for medical treatment of a major character. Women, rich and poor alike, are confined in maternity hospitals. The private blocks of hospitals are, therefore, able to count upon receiving most of the major private work of their district.

This tendency to perform all major surgical operations in hospitals relieves anaesthetists of difficulties with which we in Great Britain have to contend. The great bulk of anaesthetic apparatus is of little importance, and the clashing of appointments, and the "scurrying" from place to place, which are the bane of our existence, are not known to our colleagues over there.

Dr. John T. Hunter: I have selected two institutions on which to base my remarks—the Crile Clinic at Cleveland and the Lahey Clinic at Boston. I have chosen these because at the Crile Clinic the work is carried out by nurse-anaesthetists, whilst at Boston, anaesthesia is in the hands of really first-class men—I refer to Dr. Sise, Dr. Woodbridge, and Dr. Eversole.

The anaesthesia at Cleveland was not impressive. I watched a number of thyroidectomies and a few abdominal operations. In all cases, nitrous-oxide-oxygen was used, but I noticed that quite a quantity of ether was added during the abdominal operations. In all cases the premedication given was morphia gr. $\frac{1}{12}$ to $\frac{1}{8}$ and scopolamine gr. $\frac{1}{100}$ to $\frac{1}{150}$.

Anaesthesia in thyroidectomy.—This operation is carried out in the patient's room, with the patient in bed. The skin and subcutaneous tissues of the neck are infiltrated with novocain 1%, by a junior assistant. The nurse-anaesthetist pushes the face-piece through the bed-rails and holds it over the patient's nose and mouth. At no time is the face-piece pressed down. The mixture used is 15% to 20% oxygen. It is asserted that analgesia is produced. This happy state is assisted by a flow of light conversation by the lady-in-charge, which never ceases. No blood-pressure readings were taken and in most cases the patients were restless. A few were complaining. Endotracheal anaesthesia is never used. If an endotracheal catheter has to be passed on any particular case, it is done by the surgeon. Very little, if any, interest seems to be taken in the anaesthetic. The machine used in these cases is an Ohio.

Anaesthesia in abdominal surgery.—The same light premedication is used and the anaesthetic given is nitrous-oxide-oxygen ether. A closed circuit is used with a carbon-dioxide absorber of the circuit type. The machine employed is a Heidbrink. Blood-pressure and pulse-rate readings are charted every five minutes. The relaxation obtained was very poor. There was no sign of any individual receiving any tuition in anaesthesia.

At Boston, I visited the New England Baptist Hospital where Dr. Lahey and his assistants operate. There were three theatres but no anaesthetizing rooms. The patients were all anaesthetized in the theatre.

Pre-operative examination and premedication.—One could not fail to be greatly impressed by the very complete examination and report on the patient which was submitted to the anaesthetist before he started. A clear and lucid report of a routine examination of the heart, lungs, and abdomen was shown. In addition, a complete examination of the urine, kidney function tests, blood-count, blood-pressure, examination of sputum if any, and presence of any oral sepsis were recorded. Everything was easy to see at a glance. These examinations and reports are made in the laboratories and recorded by an interne. Actually, the copy submitted is a photostatic record of the original which is not allowed to be taken away from the Registry of the Clinic.

As far as premedication is concerned, it is interesting to observe that in all cases the dosage is very small—about half the amount used in this country. Intravenous

barbiturates are not given, and if avertin is used (and this is only on rare occasions), 0.06 grm. per kilo is the dosage. The usual premedication is morphia gr. $\frac{1}{12}$ to $\frac{1}{8}$, and scopolamine gr. $\frac{1}{160}$ to $\frac{1}{80}$. This small dosage seems to have come into use since the advent of cyclopropane. They are reluctant to give much of any drug which depresses respiration. The dose of hyoscine or scopolamine is sometimes increased in the case of very nervous patients.

Apparatus.—In almost every hospital the continuous-flow type of machine was in use. At Boston the two machines in use were a Foregger and a Connell, and the Connell is the most beautifully designed apparatus that I have ever seen.

Anæsthesia in abdominal surgery.—A new technique in spinal anæsthesia was being used in almost every case. Pontocaine (known in this country as dedicaine or pantocaine) mixed with a varying quantity of a 10% solution of glucose, was the agent used. A cannula which just pierced the intraspinal ligaments was inserted first, and then a gold needle was passed down slowly until the dura was punctured. The dose of pontocaine varies with the depth of anæsthesia and the time required, and the amount of 10% glucose solution, according to the amount of pontocaine and the depth of anæsthesia. The technique is fully described in Dr. Sise's paper entitled "Pontocaine-Glucose Solution for Spinal Anæsthesia" published in the *Proceedings of the Surgical Clinics of North America*; Lahey Clinic Number, December 1935. The advantages were a small fall in blood-pressure, anæsthesia lasting two hours, no necessity to turn the patient on the face, and control of height of anæsthesia. In a number of cases this special anæsthetic was supplemented by cyclopropane and oxygen. The resulting anæsthesia was beautiful to watch. The breathing was quiet, and the relaxation perfect. A patient who had undergone an operation for the second stage of an abdomino-perineal resection of the rectum, left the table with only a 10-point fall in blood-pressure and a pulse-rate of 86. A cholecystectomy was performed, combining a subcostal field block by the anæsthetist, using 1% novocain, with cyclopropane. The result was excellent.

Anæsthesia in thyroidectomy.—These operations were carried out under cyclopropane anæsthesia with 1% novocain infiltration of the skin and subcutaneous tissues. An endotracheal tube was passed in each case by the oral route. I asked whether they ever had any resulting tracheitis, and was told that the patients had that anyway, whether a tube was passed or not. The tube used was a metal one of the flexible type covered with rubber.

I wondered whether they could intubate by the Magill method and I found that both Dr. Eversole and Dr. Woodbridge were experts. Both took care to carry out an extensive cocaineization of the nose and pharynx with 10% cocaine. The nose having been well sprayed, two rubber tubes were passed, one through each nostril, and cocaine was sprayed into the pharynx through these. The throat was packed with wet gauze to prevent leak of gas.

Anæsthesia in thoracic surgery.—Dr. Eversole at the Lahey Clinic, and Dr. Rovenstine of New York, generally use the endotracheal method. At Boston, a flexible metal catheter is employed to prevent kinking, and intratracheal suction is applied. The closed method with carbon dioxide absorption is used in all cases to decrease respiratory movement as much as possible. Nitrous-oxide-oxygen anæsthesia has been almost entirely superseded by cyclopropane. The reasons given are as follows: (1) Extremely quiet even breathing produced. (2) High oxygen content of the mixture. (3) Non-irritation of the respiratory passages. (4) At all times the depth of anæsthesia is under the direct control of the anæsthetist. (5) Rapid return to consciousness and cough reflex, no matter how deep the anæsthesia. (6) Patients with vital capacities limited to one-quarter normal can be safely anæsthetized with adequate oxygenation, without anoxæmia, carbon-dioxide accumulation, and irregular struggling, respiratory movements.

They admit disadvantages in that the mixture is highly explosive and that nausea and vomiting do occur probably more frequently than in nitrous-oxide-oxygen anaesthesia. I inquired about the increased oozing of blood, that seems to be a drawback in these cases. Their reply was "It wasn't really any more. It only looked more."

Dr. Rovenstine is using the intrabronchial method of intubation in lobectomy and pneumonectomy in New York, at the Bellvue Hospital. I was told at the Philadelphia Congress that this is the method of choice in a number of Canadian clinics. Catheters and apparatus used, however, are clumsy and not to be compared with Dr. Magill's bronchial endoscope.

I should like to mention a demonstration of anaesthesia in thoracoplasty, given by Dr. Harold Bishop, anaesthetizing for Dr. Behrend at the Philadelphia General Hospital. Cyclopropane was again used, the reasons for this choice being similar to those given by Dr. Eversole. Premedication was light, as at Boston. The induction was slow and smooth. The apparatus used was a Foregger with a circuit absorber. No endotracheal catheter was passed. Anaesthesia was smooth throughout and there did not seem to be any excessive haemorrhage. The patient did not seem to be much disturbed at the end of the operation. Dr. Bishop said that he had been using cyclopropane on these cases since 1934, and that in a series of 646 patients, there had been no deaths during anaesthesia and no deaths after operation that could have been attributed to the anaesthesia. Shock occurred in seven cases, retention of urine in three cases, distension of the abdomen in five cases, and nausea and vomiting in 45 cases.

Another anaesthetic agent in use is divinyl ether. Dr. Marvin of Boston is expert in its administration. The apparatus used is, again, a Foregger, with a special attachment so that the vinethene may be introduced into the closed circuit drop by drop, until the requisite depth of anaesthesia is obtained. It is used with nitrous-oxide-oxygen. Dr. Marvin claims quick recovery and absence of nausea and vomiting.

The position of the anaesthetist in America, from a financial point of view, may not be so good as in London, but he certainly has behind him the full support of his clinic as regards opportunities for research. He has all the laboratories at his disposal and no idea put forward is ever too trivial to be considered and fully investigated. In England the anaesthetist, if he wishes to construct an apparatus of his own design, has to bear the burden of the cost himself. In America the cost is borne by the clinic, and the apparatus is constructed by engineering companies of great experience, who can turn out really beautiful work at a minimum cost.

Dr. W. Stanley Sykes: For efficient organization, teaching, and research, and for boundless enthusiasm and faith in the future of our craft, it would be difficult to find a better place than Madison, Wisconsin, where Ralph Waters is the Head of the Department.

Pre-operative routine at Madison.—The anaesthetist visits every case before operation and fills up a complete record of the patient's condition. At the same time he decides upon the method to be used, and orders whatever preliminary medication he thinks fit. This examination ensures that a record is kept which will be of real value for statistical purposes, and it also allows the anaesthetist to estimate the risk he is to undertake and to obtain valuable information which affects the choice of technique.

Procedure during operation.—Blood-pressure readings are taken as a routine so that the patient's condition, already familiar to the anaesthetist, is constantly under observation. These readings, as carried out in this hospital, are no trouble to the anaesthetist. The sphygmomanometer arm-band and the stethoscope tambour

are strapped into position beforehand by the porter, and the arm-band is automatically inflated by the gas machine when necessary. The manometer itself is safely fixed on the machine out of harm's way. The blood-pressure readings, together with many other details, are charted as the operation proceeds.

Post-operative routine.—All cases are seen by the anaesthetist after operation and the visits are repeated, if necessary, for the completion of the record sheet. He is also called in to see any cases of post-operative anaesthetic complications. This follow-up work is of great value in the important question of risk-estimation.

Records.—The record sheets find their way, when complete, to the anaesthetist's office. Here, by means of a simple little machine, a card is punched to correspond with each one. The record is then bound with the case papers and the card filed. Each card contains 450 positions for punch-holes, so that an enormous amount of information can be recorded. Any desired information can be extracted from the cards by passing them through a sorting machine.

Research.—Each anaesthetist is responsible for reading certain journals and publications from which he picks out and summarizes articles of anaesthetic interest. The whole staff is thus kept informed of recent work. A great deal of work is done jointly with the Physiological and Pharmacological Departments. It was at Madison that the carbon dioxide absorption method was developed. It was here that cyclopropane was introduced after several years' work on animals.

Tuition.—This is very thorough. All students are put through a course of anaesthesia on animals before being allowed to try their hands upon human patients. Wisconsin students then devote five weeks full time to human anaesthesia.

Equipment.—Anaesthetic gases are piped to the theatres from a central supply room. The Department of Anaesthesia has also charge of the oxygen therapy and resuscitation apparatus. Oxygen has been laid on to 100 beds. There is also a Drinker respirator.

At the Wisconsin General Hospital in the years 1933-36 there were 10,638 cases of inhalation anaesthesia. The total death-rate was 3.33%. At an English general hospital where the surgery is considered to be first rate, but anaesthesia is unorganized, the average death-rate over seven years—covering about 60,000 cases—was 4.28%—nearly 1% higher than at Madison.

To bring the importance of small percentages home to the average surgeon one may quote the figures of a third general hospital, also English. It is situated in a town of about 100,000 population, and is staffed entirely by the local panel practitioners, with the exception of one specialist for eyes, ears, noses, and throats. Here we have purely general practitioner surgery, with none of the complicated hierarchy or prestige of a teaching hospital. The types of operation are much the same—anything is taken—and the mortality works out at 5.3%. Take away the specialist surgeons and give their work to the G.P. operator—and the adverse balance is again only 1%. It would appear then that the importance of first-class whole-time anaesthesia is equal to the importance of first-class whole-time surgery. Such is my statistical justification of the Madison organization.

Mr. I. W. Magill said that anaesthetists in North America had many advantages over British anaesthetists. There, an anaesthetist usually attended a hospital in which most of his work was done, without the necessity of transporting apparatus, or of wasting time in travelling from one place to another between cases.

He had been impressed with the facilities for research. At the Mayo Clinic the co-operation of experts was available in every branch of scientific investigation. Dr. Lundy had his own private dissecting-room for research and for tuition of regional methods.

With regard to nurse-anæsthetists : although emphatically opposed to persons without a medical qualification giving anæsthetics, he (Mr. Magill) felt that the system at the Mayo Clinic was worthy of unbiased examination. There were not sufficient qualified anæsthetists to cope with the surgical work. Besides a first-class nursing qualification, the nurses selected were required to show, by their intelligence, a particular aptitude for the work. They attended lectures and demonstrations for one year before being allowed to begin practical work. Even then, intubation and regional anæsthesia were reserved for qualified experts.

Section of Ophthalmology

President—W. H. McMULLEN, O.B.E., F.R.C.S.

CASES SHOWN AT ST. THOMAS'S HOSPITAL, LONDON, MARCH 12, 1937

Transitory Tremulous Lens.—M. E. ALVARO, M.D. (Sao Paulo, Brazil).

The patient, a man aged 29, was first seen with uveitis in his left eye. He gave a history of two previous attacks, which had been treated as being syphilitic, although the Wassermann reaction had been negative. The vision in the affected eye was reduced to counting fingers at 3 ft. There was much exudate in aqueous and vitreous and there was slight hypotension—as compared with the other eye.

Protein was injected intramuscularly and atropine was prescribed. X-rays showed several foci of dental sepsis. General examination for other foci and for tuberculosis was negative.

The dental foci were removed and after six injections of protein, both aqueous and vitreous began to clear. Vitamins A and D, with calcium, were prescribed and the vision gradually improved to $\frac{6}{60}$. Suddenly, seven weeks after the first examination, the condition relapsed. Vision went down to light perception, and both aqueous and vitreous were almost opaque with exudates. At that moment iridodonesis and tremor of the lens could be easily seen and led us to think that the lens had been dislocated.

The tremor of the lens increased during the next few days and then gradually decreased, disappearing entirely nine weeks after it had first been seen. At the time of the disappearance of tremor of both iris and lens, the exudates in the aqueous and vitreous had partially cleared and the fundus became visible, showing organized vitreous exudates adherent to the retina. Vision gradually improved to $\frac{6}{36}$.

Five weeks later the vision decreased suddenly and a large retinal detachment was found. A tear in the retina was easily located in the 2 o'clock meridian, 40° from the posterior pole of the eyeball. Safar's operation was performed, with good results. The retina is now, seven months after the operation, completely re-attached and vision has reached $\frac{6}{12}$.

I have found no reference to transitory tremulous lens in the ophthalmological literature available. Iridodonesis combined with tremulous lens has been generally considered as true evidence of a dislocated lens. Recently, however, A. W. D'Ombrain, in the *British Journal of Ophthalmology* (1936, 20, 22), described a case in which there was a tremulous lens without iridodonesis, which led him to regard the case as not being one of dislocation. In my case there could be no question as to the absence of dislocation. The fluidity of the vitreous might have been the cause

of the tremulous lens, as has been suggested by D'Ombrian. In the case I have just described, as in his, the intra-ocular tension was lower than normal, and in my case the vitreous could be seen through the transparent lens and showed increased fluidity. The fluidity of the vitreous cannot, however, fully explain the tremulous lens for, as we all know, the normal lens shows tremor during extreme accommodation, even with normal vitreous and, conversely, in many cases of very fluid vitreous, there is no tremor. In the present case there must have been some other cause for the marked tremor of lens and iris; possibly, as a sequel to the inflammation of the choroido-retinal tract, the longer posterior fibres of the zonule were affected, thus loosening the lens. Those fibres, after the inflammation had passed, regained their former tension, and brought the lens back to its normal position.

Congruous Field Defects due to Congenital Absence of Nerve-fibres.—

P. G. DOYNE, F.R.C.S.

F. S., female, aged 1 year.

Absence of upper central part of binocular field recently noticed.

R.V. = $\frac{6}{36}$ not improved. L.V. = $\frac{6}{6}$.

Practically congruous field defects extending from the blind spots over the upper nasal and part of the upper temporal quadrants. No evidence of past intra-ocular disease. Symmetrical pits in lower part of both optic discs associated with pigment proliferation. Neurological examination negative.

Retinal Changes in a Case of Purpura.—P. G. DOYNE, F.R.C.S.

M. P., female, aged 10.

Spleen removed on account of purpura hæmorrhagica in December 1936, since when sight of both eyes has been weak.

First seen at St. Thomas's on January 18, 1937. R.V. = $\frac{6}{36}$ and L.V. $\frac{6}{12}$. Both optic discs surrounded by retinal hæmorrhages in nerve-fibre, layer partially covered by white fibrinous matter. Central retinal œdema and hyperæmia. Star figure at left macula.

15.2.37: R.V. = $\frac{6}{9}$ partly. L.V. = $\frac{6}{12}$.

Fundi much clearer. Exudate less. Nummular pigmentary deposits around optic discs. Hæmorrhage resolving. Macular star figure disappearing.

? Hæmorrhage from Vascular Growth of Orbit.—J. E. M. AYOUB (for P. G. DOYNE, F.R.C.S.).

William C., aged 53, electrician.

History.—During the Great War he was stunned in an explosion, but suffered no immediate injury beyond this. For some time afterwards he had headaches, which disappeared spontaneously. From about 1929 until one year ago he noticed that when he bent down his vision became blurred and that it slowly righted itself when he straightened himself up again. He thought that the right eye disappeared behind the upper lid when he stooped, but at no other time. He was examined by Dr. J. St. C. Elkington in October 1935. The right eye was slightly prominent, and bending to the right or forward brought on the abnormal movement upwards of the right eye. A vestibular cause was excluded. During the last year he has not noticed the phenomenon again. At the beginning of February 1937, during a space of four hours, the right eye became fixed and began to push forwards.

Pain was moderate. Sight diminished considerably. No headache. There has never been tinnitus.

On examination.—Marked exophthalmos. Chemosis +; ptosis. Limited external movements in all directions, the least upwards. Right pupil oval; medium dilatation; sluggish light reaction. R.V. $\frac{6}{24}$; L.V. $\frac{6}{8}$. Retinal veins congested. Dilated vein in the right lid.

Progress.—Three days after admission some ecchymosis was noticed in the lower lid. The proptosis had decreased, the pupil was normal, and vision had improved. Pulsation or thrill was never elicited at any time. Movements of the globe were fuller, especially upwards and outwards. The right eye was displaced upwards, in comparison with the left. Since then the condition has steadily improved. One week ago R.V. and L.V. = $\frac{6}{8}$. Diplopia was noticed only to the right and downwards, owing to limitation of movement of the right eye. The eye also was less displaced upwards and was not proptosed.

Investigations.—X-ray: Sinuses, orbital foramina, and right carotid arterial system all negative, as outlined by a thorotrast injection into the right internal carotid artery by Mr. R. H. Boggon. Blood-pressure 110/80. Pulse-rate 72 to 80. Nothing abnormal found clinically in chest, thyroid region or central nervous system. A skiagram showed abnormality of the right superior orbital fissure. Examination by Hess's charts suggested underaction of a combination of muscles.

Uveo-parotitis.—J. E. M. AYOUB (for P. G. DOYNE, F.R.C.S.).

Mrs. C. K., aged 23. Para 1. Under the care of Sir Maurice Cassidy.

Has had mumps; is normally healthy. No history of tuberculosis in a large family. A lodger has had "dry pleurisy".

On January 15, 1937, she suddenly noticed a left facial paralysis after having twenty-four hours of pain below and behind the left ear. Three weeks later the right facial nerve was affected. At the same time vision became misty. Soon after this both parotid glands became much swollen but were not very painful. She had previously been quite well except for occasional headaches, and had noticed no debility or skin affection.

On admission.—Severe bilateral facial paralysis. Both parotid glands swollen, left more than right, and firm lobulation could be distinguished. Mouths of Stenson's ducts, especially left, both injected.

Upper cervical lymphatic glands somewhat enlarged, but soft and ill-defined.

Bilateral irido-cyclitis, left more than right. No nodules on irides. K.P. on both corneae. Hazy vitreous bodies. No suggestion of optic neuritis.

Investigations.—Mantoux, Wassermann, and Sachs Georgi reactions negative.

X-ray examination: Heart, lungs, and paranasal sinuses, appeared to be normal.

Blood-count: Erythrocytes 5,420,000; Hb. 92%; leucocytes 6,360. Blood-film: Polys. 45%; small lymphos. 27%; large lymphos. 12%; large hyals. 27%; eosinos. 1%.

? Choroidal Growth.—T. E. DAVIES.

The patient, a healthy woman, aged 26, called on me about three months ago to be refracted. With glasses $\frac{3}{4}$ was obtained in each eye.

The left retina was normal, but in the right retina a dark grey area came to within about a disc's diameter of the macula and extended into the upper and

outer quadrant as a rounded mass about four disc diameters across. It was raised four diopters. Surrounding the area were a few scattered patches of rarefied atrophic retina. Between these and the extreme periphery the retina appeared to be unaffected. The vitreous was quite clear, and no other abnormality of any sort was detectable. The intra-ocular tension was normal. There had never been any pain. In the charts of the visual fields was a large scotoma corresponding in size to the mass, and sharply delineated. The intact retina between the mass and the periphery could be plotted, so that at the nasal limit of the field the scotoma was bordered by a tongue-like elongation of the field vision. The Wassermann reaction was negative.

During the last three months the swelling has become very slightly larger and the atrophic areas at the lower limit are now detached. A very slight oedema of the macula has developed. The vision now is a partial $\frac{6}{60}$ and the patient is still comfortable.

While concluding that this mass (which lies too far back for ordinary transillumination) must be a solid detachment, and presumably a choroidal melanotic sarcoma, the possibility of its being a form of cyst into which hæmorrhage has occurred has been considered. In support of this latter diagnosis, the rarefied patches were regarded as being the outskirts of a large area of old choroido-retinitis.

The clear media and the absence of similar patches elsewhere in either eye tend to detract from the cyst diagnosis. In any case removal of the eye is the safest course.

? Sarcoma of the Choroid. ? Retinitis Exudativa Externa.—EUGENE WOLFF, F.R.C.S.

W. W., a man aged 41, was first seen at the Royal Westminster Ophthalmic Hospital on October 28, 1936, complaining of mistiness of the left eye for three weeks.

On examination.—Right eye: Normal; vision $\frac{6}{60}$ partly. Left eye: Vision $\frac{6}{60}$ partly; fundus shows extensive subhyaloid hæmorrhage upwards and nasally. General investigation, including Wassermann reaction, negative.

30.1.37: The hæmorrhage had absorbed leaving a raised whitish mass in and up from the disc. The edges rise sharply from the surrounding retina. The retinal vessels disappear beneath the mass to reappear above and nasally. Transillumination negative.

This case may be similar to those cases of choroidal sarcoma described by Professor Renne in the *Transactions of the Ophthalmological Society of the U.K.* 1936, 56, 270. These are characterized by the fact that the patient when first examined has a vitreous hæmorrhage which obscures the fundus details and only later, when this clears up, is the tumour seen. The hæmorrhage tears through the retina so that the growth fungates freely through into the vitreous and explains how the retinal vessels may run deep to the growth.

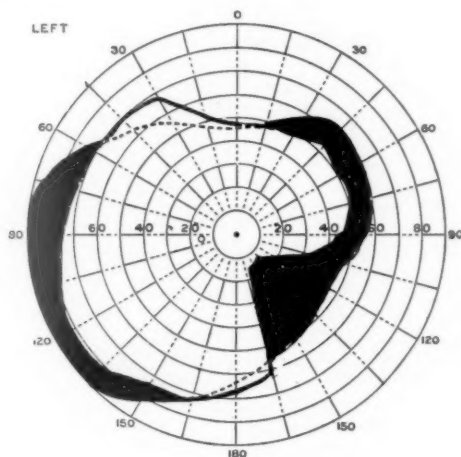
One has not, however, been able to exclude a mass formed by changes in the blood-clot (retinitis exudativa externa), and at the moment the case is being watched, especially for any increase in the scotoma.

Juxtapapillary Choroiditis (Jensen).—J. D. MARTIN-JONES, M.B., B.Chir. (for EUGENE WOLFF, F.R.C.S.).

Miss L. A., aged 23.

Seen at the Royal Westminster Ophthalmic Hospital February 20, 1937, complaining of misty vision in the left eye for ten days.

On examination.—Right eye normal; vision $\frac{6}{6}$ unaided. Left eye: vision, hand movements. Slight ciliary injection. Pupil sluggish to light directly—reacts normally consensually. Fine keratitis punctata present. Vitreous opacities. The disc edges are oedematous—especially temporally, and there is a white patch of exudate adjacent to the supero-temporal margin of the disc, partially obscuring the underlying vessels.



The field of vision shows a lower nasal sector-shaped loss.

General examination.—Nothing abnormal discovered; no staphylococcal lesions obvious.

Special investigations.—Ear, nose and throat: Empyema of maxillary antrum. No evidence of dental sepsis. Wassermann reaction negative. Von Pirquet reaction weakly positive. Urine: no abnormality found.

[November 13, 1936¹]

Delayed Corneal Ulceration following Mustard Gas Burns.—FRANK HECKFORD, L.R.C.P., M.R.C.S., D.O.M.S.

J. S. P., male, aged 41.

History.—Exposed to mustard gas during the War; some time passed before he received treatment. He spent many months in hospital with the "eye trouble". Eventually he appeared to be cured.

He complained of no symptoms until August 1932.

Present condition.—Porcelain-like appearance of the conjunctiva. Bunches of conjunctival vessels of irregular calibre. Loss of substance of the cornea. Vertical folding apparently in Descemet's membrane. A crystalline effect in the substance of the cornea is seen with the slit lamp. Corneal sensation unimpaired except over the actual destroyed areas. Fundi: Nothing abnormal seen.

R. V.: $\frac{6}{36}$ with + 0.50 sph. and + 1.0 cyl. axis $18^\circ 60^\circ = \frac{6}{18}$. L. V.: $\frac{6}{36}$ with + 3 cyl. $\angle 45^\circ = \frac{6}{24}$.

¹ Transferred from January report.

Tubercle on the Free Border of the Iris.—T. M. TYRRELL, F.R.C.S.

A. P., a woman, aged 28, married.

No family history of eye trouble.

History.—First seen July 20, 1936, complaining of pain and dimness of vision for one month. Wassermann reaction negative; heart and lungs normal; phthisis suspected last year, but this has not been confirmed by X-ray examination on two occasions.

Examination.—In July a pink gelatinous nodule appeared on the free border of the iris at 4 o'clock, about 2 mm. in diameter; one large patch of keratitis punctata at the centre. Slit-lamp shows one or two posterior synechiæ. Now, after two months' treatment, the mass is 1 mm. broad, and has puckered up the iris on the left side; two more small masses of keratitis punctata above the original one.

Treatment.—Atropine drops 1% and injections of T.R. weekly, commencing with a dosage of 1/10,000 mgm. The tubercle is slowly getting smaller.

(From Mr. H. S. Worton's Clinic, Princess Beatrice Hospital, S.W.5.)

Discussion.—Mr. J. FOSTER said that the appearance of this condition by focal illumination suggested that it was a gumma rather than a tuberculous lesion. It was situated on the pupillary, and not on the ciliary, margin, it was rather large, and was of a yellowish-red, rather than a greyish-red colour.

Mr. EUGENE WOLFF said that in the clinical diagnosis the number of vessels was very important. The relatively avascular type was likely to be tuberculous. If the condition in the present case had been gummatous, vessels would have been evident. He did not consider that the localization on the pupillary or ciliary border had any bearing on diagnosis; tuberculous lesions, and also secondary lesions in syphilis, occurred on both sites.

Section of Medicine

President—Sir CHARLTON BRISCOE, Bart, M.D.

[February 23, 1937]

DISCUSSION ON MILK AS A FACTOR IN THE CAUSE OF DISEASE

Dr. William G. Savage: As long ago as 1857, when Dr. Taylor of Penrith demonstrated that an outbreak of typhoid fever was spread by milk, the possibility of milk acting as a vehicle of infection was apprehended, but it took many years for the medical profession to realize its intimate significance. At this time it is unnecessary to advance evidence of what is so completely attested, and my task is rather to try and estimate the risk of infection from this source, to demonstrate the paths of infection, and to mention any contributory factors which influence infection.

To us who have been trained in a bacteriological atmosphere the peculiar significance of milk as a vehicle of infection seems obvious, since three contributory factors operate. (1) The cow may suffer from many infections and some of these are transmissible to man through her milk. (2) Milk is a suitable medium for the multiplication of most pathogenic bacteria so that, should a few gain access, those few rapidly multiply and constitute an infective dose. (3) Lastly the extraction of milk from the cow, and the various stages through which it passes before it reaches the consumer, involve much human handling and facilitate the transmission of infection to the milk from human sources, should those who handle the milk be in an active or a passive infective condition. It will be convenient to consider infections from these points of view.

HUMAN INFECTIONS ASSOCIATED WITH INFECTION OF THE COW

(1) *Tuberculosis*.—Since bacteriologists can differentiate the type of tubercle bacillus in individual cases from which suitable material is obtainable, we are in a position to determine with considerable accuracy the proportion of human tuberculosis which is of bovine origin: This we can assign to milk and milk products since tuberculous meat infection is relatively negligible. Applying the ascertained bacteriological findings to our Public Health Statistics I made such a calculation in 1929 in my book "The Prevention of Human Tuberculosis of Bovine Origin". A special Tuberculosis Committee of the People's League of Health (1931) reinvestigated this problem and produced very similar figures. I brought the figures more up to

date in my Mitchell Lecture (1933), and the following table is taken from that lecture :—

YEAR 1931.								
Type of tuberculosis	Deaths under 5 years	Per-centage bovine	Calculated deaths of bovine origin	Deaths over 5 years	Per-centage bovine	Calculated deaths of bovine origin	All ages calculated bovine deaths	
Respiratory	303	0	0	29,355	1	294	294	
Nervous	1,286	34	437	1,312	20	262	699	
Abdominal	291	80	235	800	33	267	502	
Generalized	327	25	82	971	9	87	169	
Other varieties	55	20	11	1,115	5	56	67	
All kinds	2,262	33	765	33,553	2.9	966	1,731	

The profession owes a deep debt to Dr. A. S. Griffith for his prolonged and unflinching work in isolating and determining the type of bacillus from so many cases, and all these calculations are mainly based upon his work.

There is evidence that, in our anxiety not to overstate the case, we have understated it. In recent years it has been demonstrated that the proportion of pulmonary tuberculosis of bovine origin may be materially higher than that given in the table. In some series it has been as high as 2 or 3% (Bradford) and in parts of Scotland considerably higher, while quite recently Griffith and Smith (1935) found in north-east Scotland 13 pulmonary tuberculosis cases bovine, out of 103 examined (12.6%). Also Griffith and Menton (1936) found, in Staffordshire, the bovine proportions in other types of tuberculosis much larger than those usually accepted.

We can accept as a minimum statement the conclusion in the Report of the People's League of Health :—

"In England and Wales about 6% of all deaths from tuberculosis are caused by the bovine type of bacillus. About 2,000 deaths in England and Wales, mostly in children, occur annually from this cause. At least 4,000 fresh cases of bovine infection develop each year, an immense amount of suffering, invalidity, and often permanent deformity, being thus caused by this bacillus."

Limits of time will not allow me to elaborate, but facts ancillary are the following : On an average 40% of our milch cows are infected with the tubercle bacillus. About 0.2% of all cows (1 : 500) are suffering from tuberculosis of the udder and excreting large numbers of tubercle bacilli into the milk. The percentage of raw milk containing living virulent tubercle bacilli varies in different parts of the country, but a fair average is 6 to 7%, while in bulked raw milk as sent to large centres the tubercle bacillus can be found in every sample.

(2) *Undulant fever*.—Contagious abortion of dairy cattle is common, and the associated organism (*Brucella abortus*) was isolated in 1897 by Bang and named the *Bacillus abortus*. As an illustration of its prevalence Priestley's work (1934) may be quoted. He examined sera from different animals, including 1,210 from cattle, and concluded that in this country not less than 20% of the cows have antibodies specific to *Brucella abortus* in their blood. This incidence is considerably higher in cows than in heifers or steers, as might be expected.

The incidence of the disease varies widely as between different herds, and for example Orr (1932), in nine different herds, found the percentage to vary from 0 to 65%.

Many series of raw milk samples have been examined for *Brucella abortus*, with positive findings in 8 to 10%. It is important to recognize that high-class milks show no lower liability to infection. For example Pullinger (1934) records that of

101 samples of milk from 45 tuberculin tested herds, while only one contained tubercle bacilli, *Brucella abortus* infection was demonstrated in 70. With bulked milk from 3,000-gallon rail tanks, 53 out of 63 were contaminated with this organism. Of 105 ordinary milk samples from Cheshire 39 contained *Brucella abortus* and of 104 from Somerset 20 were positive.

As regards the incidence of undulant fever in man, Dalrymple-Champneys (1929), in a valuable survey of the subject, could then only find records of 14 well-authenticated cases originating in England. In a subsequent paper (1933) he gave an account of 115 authenticated cases in England and Wales. These resulted in four deaths and 1,113 weeks of fever. Wilson (1932) summarized particulars of 136 cases of which 94 were in England and Wales, 31 in Scotland, and 11 in Ireland, but of course not a different series from those of Dalrymple-Champneys. He discussed various serological findings and concluded, "On the basis of serological investigations it is calculated that probably 500 cases of undulant fever occur annually in England and Wales".

It will be obvious that there is a discrepancy, even if we accept Wilson's estimate of 500 cases a year, between the comparative fewness of undulant fever cases in man and the widespread opportunities to be infected as shown by the high proportion of infected milks. We have to appreciate that numerous workers (Wilson, Smith, Dible, and Pownell amongst others) have shown that veterinarians and farm workers and others coming in contact with infected animals show evidence of a good deal of infection, usually latent. Some of the cases undoubtedly are infected by direct contact and not through milk drinking.

It is evident that man is not readily infected with *Br. abortus*, possibly the result of some latent immunity or of factors the significance of which have not been ascertained. This comparative insusceptibility does not appear to be associated with the bacterial type of infection, because the bacillus, when isolated from man, is almost always of the bovine type. Up to the present in this country the caprine and porcine strains have not been found.

(3) *Streptococcal infections*.—Mastitis, in both its acute and chronic forms, is one of the commonest infections affecting the cow. Human infection from this source is very rare. This discrepancy directed my attention to the problem as long ago as 1906, and my investigations extending over several years are recorded in three Reports of the Local Government Board. Mastitis in cows is nearly always due to a streptococcus (*Str. mastitidis*) and those studies convinced me that this strain is non-pathogenic to man. Indeed I swabbed my throat on two occasions with massive doses of this organism isolated only a few days previously from cases of cow mastitis without local or constitutional effects. I explained the known fact that certain cases of streptococcal mastitis were highly infective to man on the following hypothesis (1911):—

"Briefly stated, I regard the bovine udder and teat lesions, as commonly met with, as of purely bovine origin and, as such, harmless to man. Occasionally, either as an invasion super-added upon the original bovine lesions or as a primary infection of the milk organs, there is a local infection with organisms of human origin. In such cases the conditions present may be decidedly prejudicial to man. In other words, the cow in this class of infection, is only potentially pathogenic to man when it acts as an active or passive carrier of organisms of human origin."

This view is now generally accepted, and much additional evidence in its support has been adduced. My rather crude differentiation characters have been extended and the bacteriological differences worked out fairly fully.

Human streptococci do not readily establish themselves in the bovine udder,

as I have shown by many goat experiments, and this difficulty helps to explain the rarity of human angina outbreaks from this source.

There is a rather puzzling fact about their time distribution. In the period 1890-1910 I recorded particulars of 18 such outbreaks in Great Britain and almost certainly there were many not recorded, for the aetiological factors were not recognized. Thereafter such outbreaks were not recorded in this country, but on the other hand they began to be recorded about that time in U.S.A. and are still being recorded. When the extensive outbreak in Hove and Brighton occurred in 1929 it was by many regarded as a new type of infection although, in reality, it was quite similar to the earlier records.

Although these outbreaks are uncommon to-day we must not underestimate their importance, since they may be very widespread. In the outbreak I investigated (1905-06) at Colchester in 1905 there were over 600 cases with no deaths. In the Hove outbreak there were more than 1,000 cases with over 60 deaths. In the latter outbreak Wilkinson (1931) gives as the probable sequence: First the occurrence of a case of tonsillitis in a house visited daily by an employee of the farm, then the transference of infection by this employee to one or more cows at the farm, and finally the spread of infection both at the farm and in the town through the milk of these cows.

These outbreaks of angina are rare but serious. They are commoner in America. A study of the individual outbreaks shows that in the great majority of cases the streptococcus is derived from the udder, but in a minority the milk may be directly infected with pathogenic streptococci from human sources. In spite of much experimental work, no convincing evidence is available as to the factors which enable a human pathogenic streptococcus to invade the udder and set up mastitis.

It may be mentioned that while nearly all scarlet fever milk-spread outbreaks are due to direct milk infection from a human source, a few outbreaks are associated with udder infection. Both are streptococcal diseases, but the comparative causation frequency is exactly opposite. Not without significance is the well-attested fact that a few outbreaks of milk-spread diphtheria are associated with local teat ulceration and infection of the ulcerated areas with the diphtheria bacillus.

I do not think we have enough information to decide whether small and unrecognized outbreaks of angina in man may not be spread from these special mastitis cases, but I should think it unlikely.

(4) *Salmonella* infections.—Outbreaks of acute food poisoning, in which the vehicle is milk, occur from time to time. Most are associated with *Salmonella* infection of the milk and in many such cases it is traceable to an infected cow. I have collected particulars of 20 such outbreaks, several personally investigated. They may be extensive, as the following tabular statement of some of them shows:—

Place	Date	Cases	Deaths	Organism responsible
Newcastle-upon-Tyne	1913	523	0	<i>Salmonella</i>
Withnell and Chorley	1914	317	2	<i>Salmonella</i>
Newcastle-under-Lyme	1914	468	2	<i>B. enteritidis</i>
Glasgow ...	1914	370	0	<i>B. aertrycke</i>
Dublin (near) ...	1921	153	0	<i>B. enteritidis</i>
Kingston ...	1922	141	0	<i>B. enteritidis</i>
Aberdeen ...	1923	110	0	(not determined)
Aberdeen ...	1925	497	1	<i>B. enteritidis</i>

To take as an illustration the latest (Aberdeen, 1925) the *Salmonella* strain was found in the infective milk and subsequently in the udder and flesh of the septicæmic cow.

While the symptoms were often severe it will be noted that the case mortality is very low, i.e. 0.2% and below that for most *Salmonella* outbreaks.

(5) *Other infections transmissible to man.*—Only two need be mentioned.

While anthrax in cows is not very rare, it is so rapidly fatal to the animal that the anthrax bacillus is usually only found in the milk just before death, and it is most unlikely that it would be in milk when the animal is in any condition to be used for milk production. I have found several cases of anthrax in milking herds, but in none was there risk of the disease being spread to man by the milk, nor do I know of any cases in the literature of man being so infected. The nearest is when the milk was fed to pigs and set up the disease.

Foot-and-mouth disease in cows can be spread by milk, but very few cases, so infected, are recorded in this country. In Germany several outbreaks have been reported. The interesting outbreak in Dover in 1884 was possibly, in part, of this nature, and certainly some of the cows suffered from foot-and-mouth disease.

DISEASES SPREAD THROUGH HUMAN INFECTION OF THE MILK

Those of importance are diphtheria, scarlet fever, typhoid fever, paratyphoid fever, and dysentery. As already mentioned, sore throat outbreaks may also be so spread. The way in which the milk is infected is through a case, or carrier, of the disease in question coming in contact with the milk as a milker, or handler of the milk, subsequently.

The literature is full of recorded outbreaks, but it is most difficult to obtain data which enable us to measure the risk with any accuracy. Many outbreaks are not recorded at all, or only in such records as Annual Reports, which are not readily accessible. A study of individual annual reports of medical officers of health will furnish particulars of quite a number of milk-spread outbreaks not recorded in our journals. In other words, there are no full statistical records. Wilson (1933), for example, gives the following table, but he mentions that it represents only those cases of which he was able to collect records and probably represents merely a fraction of the total number that have occurred.

OUTBREAKS OF MILK-BORNE DISEASE IN GREAT BRITAIN, 1912-1931.

Disease	Number of outbreaks	Number of outbreaks in which number of persons affected is stated	Number of persons affected in these outbreaks
Scarlet fever and septic sore throat	31	25	3,087
Diphtheria	13	12	732
Typhoid fever, paratyphoid fever and dysentery	25	22	1,843
Gastro-enteritis	12	10	3,759
Total	81	69	9,421

The Committee on Cattle Diseases (1934) in an appendix to their report, give a list of milk-borne outbreaks reported between 1900 and 1931 in the United Kingdom and known to the Ministry of Health. The Committee remarks, "It cannot be regarded as exhaustive, for many epidemics, though recognized as being due to contaminated milk, are not reported, and many slight outbreaks of common diseases, due to milk, are not recognized as such". The list comprises: Diphtheria 14 outbreaks; scarlet fever 28; scarlet fever and sore throat 1; enteric fever 30; typhoid fever and dysentery 4; paratyphoid fever 7; diarrhoea and sickness 2; gastro-enteritis 3; sore throat 4; Salmonella infection 3. The list is far from complete, for I have notes of many outbreaks not recorded in this series.

In U.S.A. outbreaks are either more systematically recorded or are more numerous. For example Davison (1935) points out that between 1924 and 1932 (inclusive) there

have been 394 recorded outbreaks of milk-borne acute infectious diseases, and that many outbreaks are unrecorded. I might add that he states that 1,407 cases of undulant fever in man were reported in U.S.A. in 1932.

As examples of extensive outbreaks the following may be mentioned :—

Enteric fever : The very extensive outbreak in Bournemouth and Poole in 1936 of which full particulars are not yet available.

Paratyphoid fever : An outbreak of 56 cases in 1925 at Chorley. The source of infection was a case of paratyphoid fever, which was nursed at home on one of the farms supplying the milk. The Herts outbreak, in 1928, of 166 cases, had a quite similar causation.

Dysentery : The Aberdeen epidemic of bacillary dysentery in 1919, with over 1,000 cases and 72 deaths, due to unrecognized cases on the farm.

Scarlet fever : The Chelmsford outbreak of 1935, with 487 notified cases but with about 2,000 cases of illness, with 6 deaths. The source of infection was unrecognized scarlet fever at the place of production with subsequent infection of four milkers.

Diphtheria : An outbreak at Glastonbury which I investigated in 1920. As it has never been recorded in the literature, a few particulars are given below.

A milker suffering from diphtheria was removed to the isolation hospital and only discharged as free from infection after several negative swabs. He remained free from infection until his younger brother, another case, returned home after one negative swab and that from the throat only. He was evidently still infective and reinfected his brother, the milker, who slept with him and who had resumed work as a milker. Although he was recognized as a source of infection on the first day of the outbreak and was at once isolated there were 58 cases directly spread by the infected milk and a further 51 cases spread from these by case to case infection, making a total of 109 cases directly or indirectly from milk. There were 15 deaths.

A point of scientific interest in milk-borne outbreaks is the place of entry into the body. For typhoid fever, paratyphoid fever, and dysentery, no doubt it follows the usual course and infection is through the intestinal mucosa ; for scarlet fever, streptococcal angina and diphtheria, infection would be through the tonsils, while for tuberculosis there is evidence that a good deal of infection is through this route. I am ignorant of the path of entry in undulant fever and I think that this aspect deserves more consideration.

The evidence that milk is a widespread vehicle of infection is overwhelming. As regards tuberculosis, the extent of the disease so spread can be estimated with reasonable accuracy and constitutes an amount of infection which is a standing disgrace to our legislature since the remedy is known, is not difficult of application, and is only prevented from being applied by considerations which should not be allowed to weigh against the proved damage caused. For undulant fever we are gradually arriving at an estimate of the damage. For the other milk-spread infections it is less easy to assess the extent of the disease they cause, but the evidence is adequate to show that it is far from negligible. Their control, also, is less easy, since it is more difficult to close all avenues of infection, but no one can doubt that the elimination of the use of raw milk would largely get rid of these risks.

REFERENCES

- DALRYMPLE-CHAMPNEYS, W. (1929), Ministry of Health Report, No. 56.
Id. (1933), *Proc. Roy. Soc. Med.*, **26**, 1093.
DAVISON, W. C. (1935), *Am. J. Dis. Child.*, **40**, 72.
GRIFFITH, A. S., and SMITH, J. (1935), *Lancet* (ii), 1939.
GRIFFITH, A. S., and MENTON, J. (1936), *Brit. M.J.* (i), 524.

- ORR, A. B. (1932), *Proc. Roy. Soc. Med.* (Comp. Med. Sect.), **25**, 1501.
 PRIESTLEY, F. W. (1934), *J. Comp. Path. and Therap.*, **47**, 181.
 PULLINGER, E. J. (1931), *Lancet* (i), 967.
 Report of Committee on Cattle Diseases. Economic Advisory Council, 1934.
 SAVAGE, W. G. (1905-06), *Pub. Health*, **18**, 1.
 Id. (1911), *Proc. Roy. Soc. Med.*, **4** (Sect. Epid., 73).
 Id. (1933), *Brit. M.J.* (ii), 905.
 A Survey of Tuberculosis of Bovine Origin in Great Britain. Report of a Special Committee of the People's League of Health, 1931.
 WILKINSON, E. (1931), *Proc. Roy. Soc. Med.*, **24**, 1708.
 WILSON, G. S. (1932), *Vet. Rec.*, Oct. 8.
 Id. (1933), *Lancet* (ii), 829.

Dr. F. C. Minett: The present discussion has a wider scope than that which took place at the Royal Society of Medicine in 1931 [1] on Milk-borne Streptococcus Infections. I propose to deal briefly with knowledge on the subject which has been acquired since 1931, because the facts have already been published or will appear in detail shortly.

Br. abortus in milk.—The frequency with which this organism is found in milk varies widely, owing to differences in the kind of milk examined, the amount sampled, the number of guinea-pigs used and the material inoculated (cream, deposit, or whole milk), the technique used for demonstrating infection in the guinea-pig. The subject has been re-examined in detail by E. J. Pullinger (1934). He was able to reveal *Br. abortus* in 53 out of 63 samples of milk from rail-tanks, in 70 out of 101 samples of "graded" milk (from "certified" or "grade A tuberculin-tested" herds), in 39 out of 105 samples from herds in Cheshire, and in 20 out of 104 samples from herds in Somerset. The herd samples represented the product of all cows in the herd that were in milk at the time, except in the case of "certified" milk, where the samples were from a few cows only. Noteworthy points in this work were as follows. The milk from herds situated in one part of the country can be much more heavily contaminated than that from another region. The reason for this was discussed in the original article. The milk from "graded" herds, i.e. "cleaner" milk, appears to be very much more heavily contaminated than "ordinary" milk. This, it was thought, was due to "ordinary" milk having a high count of saprophytic bacteria which, when inoculated into guinea-pigs, raised the animals' resistance to the *Brucella* in the milk. Further experiments, however, showed that this was not the explanation and that the apparent lower frequency of *Brucella* in "ordinary" milk was due largely to its containing tubercle bacilli, which were, of course, absent from the graded milk. The tubercle bacillus, in fact, when mixed with *Brucella* effectually prevents the latter from invading the body of the guinea-pig [Pullinger, 1936].

Milk-borne streptococcus infections.—Dr. Savage has re-stated to-day, as he did in 1931, his views as to the importance of the cow in these infections. During the last few years, experiment and observation have provided so much support for his enlightened views that the matter is no longer hypothetical. Obviously, contamination of the milk by *Str. pyogenes* (i.e. streptococci of the "human type" or streptococci pathogenic for man) must be either *direct* (from man) or *indirect* (i.e. through the udder of the cow). I incline to the view that the *indirect* way is of major importance, and the evidence for this can be placed under three headings, (a) epidemiological, (b) cultural, (c) evidence concerned with the cow.

(a) It is unnecessary to state the evidence at length. It is sufficient to express the conclusion that widespread and continuous epidemics in man could scarcely be due to casual or intermittent contamination of milk by human beings, unless the organisms introduced could grow with fair ease in milk at atmospheric temperatures.

(b) Such information as exists is not in favour of the supposition italicized in the last sentence, but during the past year the problem has been submitted to detailed examination by E. J. Pullinger and Miss A. Kemp [1937]. As is the case with the frequency of *Br. abortus* in milk, there is no simple answer to the question of whether *Str. pyogenes* grows in "milk" at air temperatures. They included in their experiments a strain of the organism recently isolated from man, as well as a strain of "human type" freshly isolated from milk of a naturally infected cow; the temperatures used were 15°, 18°, and 22° C.; different kinds of milk were tested, viz. sterilized, pasteurized, and raw. In brief, their work has shown that while *Str. pyogenes* will grow slowly in commercially sterilized milk and especially at the higher temperatures, its multiplication in the other classes of milk, when occurring at all, scarcely becomes appreciable before the milk is passing into a state unfit for human consumption.

(c) It has been shown a number of times that cows can be artificially infected with *Str. pyogenes* by injecting small amounts of culture up the teat canal or by applying culture material to the abraded teat orifice. While such animals do not suffer from "bovine scarlatina" in the sense that such a term might be used clinically, there follows a mastitis which may be accompanied by extremely large numbers of streptococci in the secretion and by their persistence in it for weeks or months. Similarly, in connexion with human epidemics, naturally infected cows have been found on a few occasions. An instance of this occurred in connexion with the recent milk-borne outbreak of scarlet fever at Doncaster (1937). It is proposed to publish details of this and another case at a later date, but in the meantime it may be said that one of the 31 cows in the incriminated herd at Doncaster was proved to be harbouring in two quarters scarlet fever streptococci belonging to F. Griffith's Type II, i.e. the type of streptococcus found to be the cause of the epidemic. The cow in question has been acquired for further observation, but certain points of importance can be mentioned now. Infection of the right fore-quarter was associated with severe injury to the teat, which had been trodden on by another cow. It is indicated that the left fore-quarter was subsequently involved. There was a preliminary stage lasting several days, during which the cow was known to be excreting scarlet-fever streptococci in the milk, although at that time clinical symptoms were not observed. The streptococci remained in the cow's udder for at least six weeks, but fortunately during most of this time the animal was in isolation.

The question has been asked why milk-borne epidemics are comparatively rare. The reason may be that for their initiation a combination of certain factors is required and that this happens comparatively rarely. It would seem that the two most important factors are excretion of virulent hæmolytic streptococci by a milker and, coincident with this, a fresh teat injury sufficiently extensive to permit infection to take place.

REFERENCES

- BENDIXEN, H. CHR., and MINETT, F. C. [in press].
PULLINGER, E. J. (1934), *Lancet* (i), 967.
Id. (1936), *J. Hyg.*, **56**, 456.
PULLINGER, E. J., and KEMP, A. [in press].
SAVAGE, W. G., and others (1931), *Proc. Roy. Soc. Med.*, **24**, 1703.

Dr. W. M. Scott: Milk-borne diseases have commonly been divided into two groups: (1) Those in which the milk transmits to man a disease ordinarily affecting the bovine species, and (2) those in which the infection of a human disease accidentally enters milk between withdrawal from the cow and ingestion by the human consumer. In the first group are bovine tuberculosis, responsible for some thousands of human

infections per annum in this country, and brucellosis, responsible for a smaller number—but probably larger than can be proved—of cases of undulant fever. In the second group are, especially, the intestinal infections, including enteric and paratyphoid fever, bacillary dysentery in its several varieties and other forms of enteritis and colitis, and the throat infections, diphtheria—rare but well proved—scarlet fever, and non-eruptive tonsillitis with their sequelæ, the numbers of which must be very large.

More recently, however, attention has been called to a third group, that of diseases ordinarily affecting only man but transmitted to the cow and resulting in the profuse discharge of the infecting agent in its milk. In the case of scarlatinal and other streptococcal infections, the bacteriological evidence is conclusive that such a process actually occurs, but there remains the possibility, hitherto quite unsuspected, that enteric fever, though perhaps only very rarely, may also belong to this group, i.e. may become a bovine infection, so that a cow suffers from it and can transmit the disease by its milk.

One reason for suspecting the existence of this third group of milk-borne diseases—those in which infection of the cow with a human disease precedes the infectivity of its milk for man—is the degree of infection of the milk which must be assumed in some outbreaks, especially of tonsillitis, to account for its power of producing widespread disease among its consumers. Even allowing for the multiplication of the specific bacteria which may result from a small inoculation into so good a culture medium as milk, droplet infection or hand contamination by a milker or milk-handler could scarcely convey sufficient infective material to produce disease in so very high a proportion of those ingesting the milk.

These considerations apply to the large outbreak of enteric fever in August and September 1936, which produced about 800 primary cases of the disease among the inhabitants of two towns. The infection was traced to one milk supply and, so far as can be determined, to one small farm of 12 cows. The milk from these, some 20 gallons daily, was mixed with the milk of 30 other farms to a daily total of 1,600 gallons. Highly diluted as it was, this milk for three weeks was regularly producing cases of enteric fever among the consumers. No human carrier could be discovered at the farm, though a case of enteric fever developed there during the course of the outbreak and, in fact, was the first reason for fixing suspicion upon it. The water supply on the farm was bacteriologically of good quality. But it was found that the cows had as their drinking place a small river into which, about 100 yards upstream, a sewage effluent was being discharged, containing enormous numbers of typhoid bacilli: about 300 colonies of these grew per 1 ml of the sewage. It is possible, of course, and even likely, that the cows in wading into their drinking place acquired surface contamination of legs and udder, and that this contamination was conveyed to the milk in spite of the washing of the udder and teats which was a normal procedure before milking. It seems improbable, however, that such an accident could occur daily throughout three weeks and provide each day full infecting doses after the great dilution of the milk involved in bulking it with that from other farms. The same improbability seems to attach even to the supposition that typhoid bacilli, ingested by the cows with the water and surviving to be discharged in the feces, could contaminate the milk in this way, unless, indeed, the specific bacteria multiplied in the cow's alimentary canal to numbers corresponding with those in the stools of an enteric fever patient. This latter occurrence, however, would practically imply a true enteric infection of the cow and would most probably be accompanied by systemic absorption of the specific bacteria and their actual excretion in the milk. It is this occurrence which would justify including enteric fever in the third group of milk-borne diseases.

It is very regrettable, however inevitable, that in this particular instance it was

too late to get proof, either indirect, by the discovery of a cow with abnormal agglutinin content for *B. typhosus* in its blood, or direct, by isolation of these bacilli from its faeces. Attempts in both directions, some two months after the epidemic began, gave only negative results. The possibility of its occurrence is, however, of such great importance that it ought to be put to the test, and we hope, with Professor Minett's co-operation, to do this. It should be remarked, in conclusion, that there is no record in the literature of a typhoid infection of a bovine animal, except one dating back to 1902, in which apparently authentic typhoid bacilli were isolated from a spleen abscess in a cow at slaughter.

REFERENCE

- LEVY, E., and JACOBSTHAL, E. (1902), *Arch. f. Hyg.*, **44**, 113.

Section of the History of Medicine

President—E. W. GOODALL, O.B.E., M.D.

[March 3, 1937]

Medicine and Science in the Writings of Smollett

By E. ASHWORTH UNDERWOOD, M.A., B.Sc., M.D., D.P.H.

THE eighteenth century in England was a golden age for the individual. A prolonged period of unrest had been followed by an age of superficial stability, under the surface of which unchallenged abuses in all forms of corporate life were rife [1]. Merit—whether of the higher order which is genius, or of an inferior order which is akin to low cunning—very often paid, and antecedents and specialized training were by no means necessary to those who aspired to the rostrum, to Parnassus, or to the temple of Aesculapius himself. It was into this world that Tobias George Smollett was born, and it was perhaps not by accident alone that his feet were early set on the lower slopes of two peaks. There was probably more than imagination in his picture of Bramble's apothecary, who being "a right Scotsman" had always two strings to his bow and was *in utrumque paratus*.

Smollett was born in March 1721 at Dalquhurn in Dumbartonshire and received his early education at Dumbarton Grammar School. A thorough preliminary classical education there permitted him to proceed to Glasgow University at the age of 13, and there he had Cullen and William Hunter as fellow students. In a short time he was apprenticed to Dr. John Gordon and he seems to have resided in his house. Sir Walter Scott apparently believed that Smollett was a keen though somewhat mischievous apprentice. There is no reason to doubt that his early medical education was quite satisfactory. Gordon himself was a man of sound judgment and he later became one of the leading Glasgow physicians. Thirty-four years later Matt. Bramble is made to say of him in *Humphry Clinker*: "I was also introduced to Dr. John Gordon, a patriot of a truly Roman spirit, who is the father of the linen manufacture in this place, and was the great promoter of the city workhouse, infirmary, and other works of public utility. Had he lived in ancient Rome, he would have been honoured with a statue at the public expense."

A change in family circumstances compelled Smollett to relinquish his studies in Glasgow and he determined to try his fortunes in London. This was in 1739, and since Roderick Random also set out for the metropolis on November 1, 1739, we may take it that Roderick's baggage was carried by Smollett himself. A peep

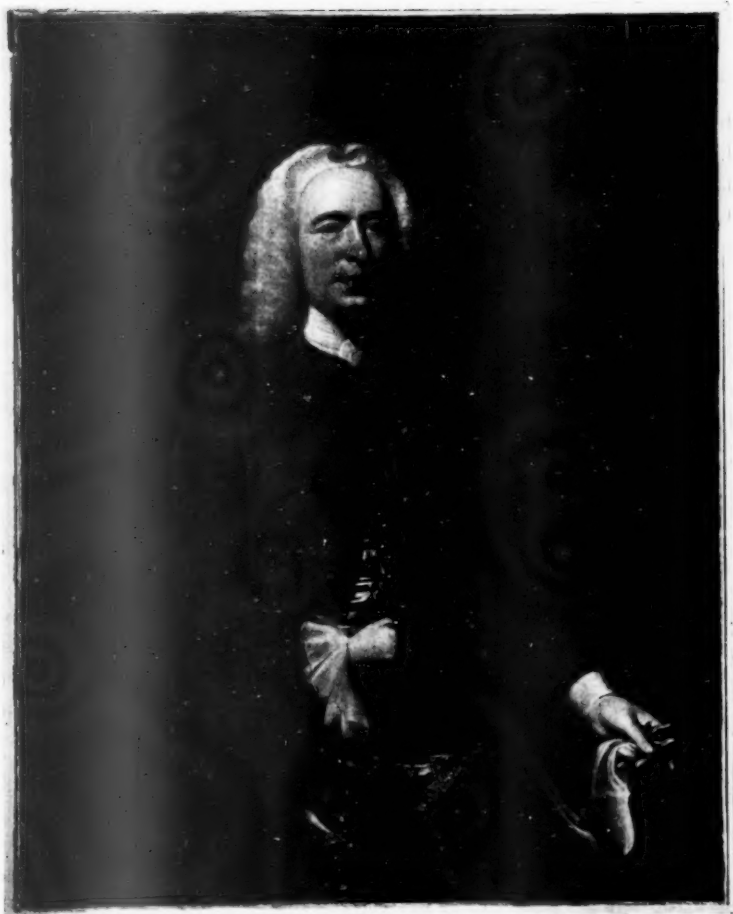
at that baggage would have revealed "one suit of clothes, half a dozen of ruffled shirts, as many plain, two pair of worsted, and a like number of thread stockings, a case of pocket instruments, a small edition of Horace Wiseman's *Surgery*, and ten guineas in cash"—and in the case of Smollett himself the manuscript of his tragedy *The Regicide*, upon which—more than "upon", shall we say? the *Surgery*—his hopes were based.

While Smollett finds his feet in the metropolis we may look at the world into which he was introduced. In politics Walpole was active, but Bolingbroke had been thrown out and was devoting himself to literature. Literature had lost Defoe, Addison, Steele, and Gay, but Swift was still writing trenchant pamphlets and Pope was elevating, amusing, or irritating the select coteries who collected in that city, which a Smollett character later called "the Devil's drawing-room". In the following year *Pamela* appeared, but perhaps Fielding had not yet thought of *Joseph Andrews*, which was not published until 1743. Johnson had no doubt recovered from the success of his *London* and he was writing much for *The Gentleman's Magazine*, where strangely enough in this year appeared his *Life of Boerhaave*, one of the greatest clinicians of his age. At this time the famous Circle had not been formed, and it would have taken more prophetic vision than the great Cham possessed to have foretold that in the following year there would be born one who, out of friendly meetings on but nine hundred days, would make of him the most living character in biography. Hume was ten years older than Smollett; Garrick was already doing well in London; but Burke and Goldsmith were mere children.

In the medical world several outstanding events had recently happened or were about to happen. In the previous year Bernouilli had stated the kinetic theory of gases—somewhat far removed from any similar theory which Smollett's characters describe. It can hardly be said that Smollett's writings evince any great love of Nature, and he was possibly not much interested by the fact that four years previously Linnaeus had published his *Systema Naturae*. Stephen Hales was busy in his vicarage. Boerhaave had just died. Albinus was adding to the work of Vesalius, and Morgagni was building up the new science of pathology. The modern study of chest diseases was unknown, for Auenbrugger was but a youth of 17, and Laennec was not yet born. In London, Fothergill had already established himself, and Mead had been Physician to St. Thomas's Hospital for thirty-six years. In this year—1739—Huxham had described Devonshire colic as a result of cider drinking.

It would appear that both Smollett's bow-strings broke during this momentous year. *The Regicide* could not find a backer, and there is no record of Smollett having done anything in practice. When we next hear of him he was appointed Surgeon's mate on board the "Cumberland", which sailed with the reserve fleet commanded by Sir Chaloner Ogle, to reinforce Vernon's fleet in the West Indies. *Roderick Random* gives a spirited description of the expedition—coloured and exaggerated no doubt, as Smollett himself asserted in a letter written in later years; but more accurate descriptions were given in his *History of England* and in his *Compendium of Voyages*. During the expedition Smollett met his future wife, Nancy Lascelles, in Jamaica—and with her the patrimony which possibly kept him from starvation for some years. On his return to England he started a practice in Downing Street, and *The Regicide* was again rescued from oblivion and accompanied the doctor on his rounds. It was the play and not the lancet which at this period took Smollett into the houses of the great. The story of this tour around the patrons is told by Melopoy in *Roderick Random*.

Smollett's practice in Downing Street does not appear to have been very successful, and before April 1746 he left it for less expensive quarters. There he lived with his wife for some time, probably until about 1750, when he removed to Monmouth House in Chelsea; this was to be his habitation until he left England for ever. *Roderick Random* appeared in 1748 and the first edition of *Peregrine Pickle* in 1751. He had



TOBIAS GEORGE SMOLLETT.

(Reproduced by permission of Colonel A. P. D. Telfer-Smollett, D.S.O., M.C., from the portrait in his possession, painted by Verelst in 1756.)



meanwhile made several visits to Bath and he appears to have had some intention of settling permanently in practice there. The two bow-strings were still twanging in unison, but it is obvious from his works that his medical practice was not thriving. The degree of M.D. to which he refers in *Humphry Clinker* went into his pocket in June 1750—granted by Marischal College, Aberdeen. In 1752 he published his one and only contribution to medical literature, *An essay on the external use of water, with particular remarks upon the present method of using the mineral waters at Bath in Somersetshire, and a plan for rendering them more safe, agreeable, and efficacious*.

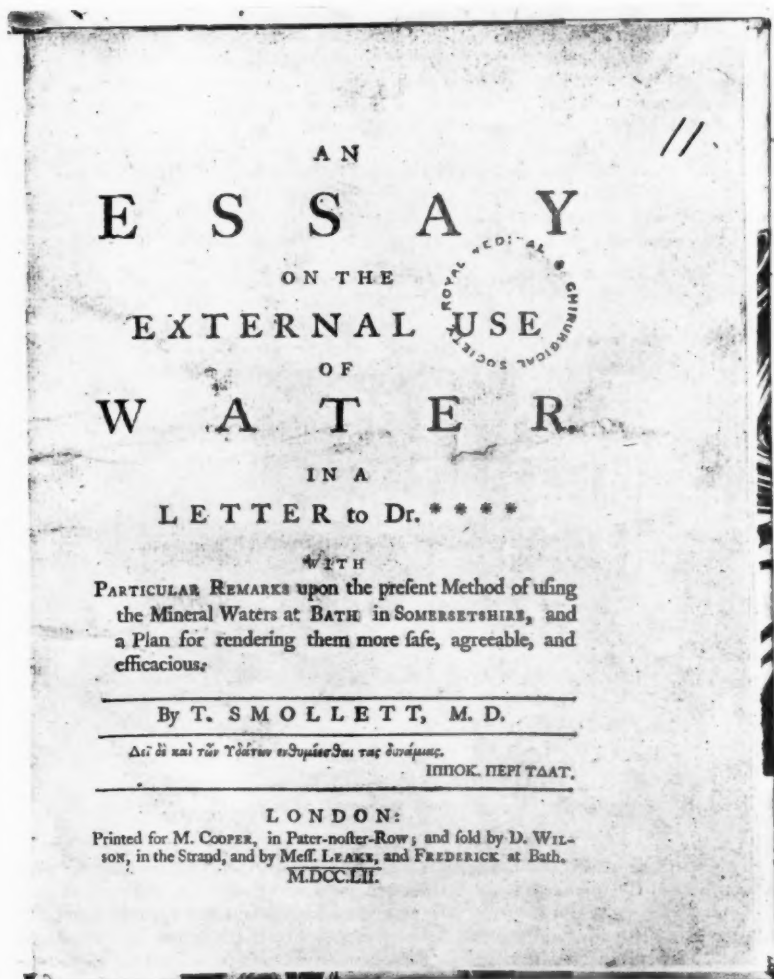
It is commonly said that this essay was the death-knell of any hopes which Smollett might have had of becoming a successful practitioner at Bath. But is this a fair statement of the facts? It is asserted that he affirmed his disbelief in the efficacy of the spa waters and that therefore the fashionable clientèle who visited Bath and other spas would be little likely to patronize him. In effect the *Essay* appears to be an indictment of crying abuses which undoubtedly existed, and a well-reasoned summary of measures which might be adopted for their correction. Here in Bath—



MONMOUTH HOUSE, CHELSEA.

(Reproduced from Beaver's *Memorials of Old Chelsea*).

“the great hospital of the nation”, as he calls it—we find the elementary principles of hygiene flagrantly disregarded. “Diseased persons of all ages, sexes, and conditions”, as he tells us in the *Essay*, “are promiscuously admitted into an open Bath, which affords little or no shelter from the inclemencies of the weather”. The bathers are exposed to prying eyes and, in addition to the danger of infectious distempers, they are nauseated by the filth, “which, being washed from the bodies of the patients, is left sticking to the sides of the place”. The King’s and Queen’s Baths had been known to contain forty-five patients at one time. Eighteen years later Bramble in *Humphry Clinker* is still complaining of the inconveniences and dangers of the place, though he admits that premature old age may be colouring his judgment. Bath may still be a “National Hospital”, but one would imagine that none but lunatics are admitted. There is still the mischief due to wet chairs, and he was disgusted at the sight of a child “full of scrofulous ulcers, carried in the arms of one of the



TITLE PAGE OF THE ESSAY.

guides, under the very noses of the bathers" [2]. Bramble does not even exonerate the drinking water, since he suspects that there is, or may be, some regurgitation from the bath into the cistern of the pump [3].

Examples of his views on Bath can easily be multiplied from his works. Of the *Essay* it is sufficient to say that although the reasoning and the practical suggestions received the support of Mr. Cleland, a prominent surgeon in Bath, and are worthy of respect for their intrinsic value, the physiological argument which precedes the more practical part shows that Smollett was still in the leading strings of the ancients. In a word, it shows no evidence that the author was possessed of a scientific mind. The description of the cure of wens by the application of the hand of a person who had been hanged, cited not as a superstitious belief but in all seriousness, savours more of a page from *Count Fathom* or *Sir Launcelot Greaves* than a scientific treatise calculated to advance the author in his chosen profession.

Smollett appears to have given up the practice of medicine shortly after the appearance of the *Essay*. He continued to reside at Monmouth House and there he was visited by numerous friends who benefited materially from his generous though somewhat surly disposition. His *systema nervosum maxime irritabile* was a source of anger to his enemies, of discomfort to his friends, and of regret to himself. *Ferdinand, Count Fathom* appeared in 1753 and from that date he became a professed man of letters, his generous disposition causing him not infrequently to wait with anxiety for his wife's allowance from Jamaica. Yet he had his monetary successes. His *History of England* was an unqualified success and was said to have brought him in a sum of £2,000. He later founded the *Critical Review*, the first number of which contained Dr. James Greaves' *A Cornelius Celsus of Medicine* and Huxham's *Observations on Antimony*. There is no doubt that he edited for the Press certain medical works of his time, such as the first part of Smellie's *Midwifery*, and some at least of the notes on medical books which frequently appeared in the *Critical Review* were from his hand. Increasing ill-health, due to overwork, drove him abroad in 1763, and his tour of France and Italy, most interestingly described in *The Travels*, lasted two years. We read of the scorbutic ulcer on his hand, to which he also referred in a letter to William Hunter [3a]. His asthma is often very troublesome, and it is evident that he is a man prematurely past his prime. For some years after his return he continued his literary work, but in 1769 he went abroad again. *Humphry Clinker*, by many considered his finest work, appeared just before his death at Leghorn in September 1771.

From available material it would seem that the greater part of thirteen years of Smollett's life was passed, at least intermittently, in the practice of his profession. During the last eighteen years of his life medicine was to him a memory of an effort—perhaps even of a failure. Yet these early years imprinted on his work the unmistakable impression of a man who knew the medical profession from within. To parody a famous Latin epitaph, we might say that there was nothing which he touched which he did not medicate. Even when he is writing in his most "rollicking" mood, as Hazlitt would have said, there is something in his descriptions which marks the man who has himself handled patients and treated their maladies. So definite is this feature that it might be used with some confidence as a weapon of criticism. For example, the second edition of *Peregrine Pickle*, published in 1758, contained the rather sordid and boring *Memoirs of a Lady of Quality*. At the time of publication it was no secret that the *Memoirs* were authentic; it was no secret also that the author was the notorious Lady Vane. Commentators usually assert that the *Memoirs* were written by her Ladyship, with the assistance of Dr. Shebbeare, and that they were considerably edited by Smollett himself. In these hundred odd pages there are four references to incidents of a medical nature. Smollett himself would probably have increased these considerably. Further, only one of these incidents is such that it could not have been described equally well by any person of moderate education;

the exception being where Lady Vane says that "my disorder recurred with such violence, that I was obliged to send for a physician, who seemed to have been a disciple of Sangrado; for he scarce left a drop of blood in my body" [4].

In the few papers which have appeared on the medical aspect of Smollett's writings, the emphasis is usually placed on his descriptions of conditions in the Navy of his time, and on his observations regarding the unhygienic state of Bath. In these passages Smollett was writing as a reformer, and they are consequently of great interest and importance. But scattered throughout his literary works and his letters are numerous shorter passages which are equally important in assessing his relationship to the medical views of his day. No complete study has ever been made, and in the time at my disposal it is possible to use only a small portion of the material available. I shall therefore deal only with the more important allusions, dividing them broadly into those which deal with the work of the apothecaries, the surgeons, or the physicians. To avoid repetition I shall say little regarding his observations on life in the Navy and his notes on Bath. For these subjects the student is referred to the papers by Drinker [5], Beck [6], and Jones [7].

(a) *Anatomy, pathology, and surgery.*—Anatomy and pathology are very poorly represented in the writings. Mr. Lavement, the apothecary, is described as having remains of teeth "which consisted of four yellow fangs, not improperly, by anatomists, called *canine*" [8]. It is interesting to note, in relation to the belief of the ancients that the seat of the soul was the pineal gland, that the Atom which told its story to Nathaniel Peacock was situated in this organ [9]. In its early existence it had taken up its habitat in "the nervous plexus situated at the mouth of the stomach of a fat alderman". In the same work the word *podex*, for long used only in a zoological sense, is applied to a human being [10]. Muraciami's brain is described as being "full and compact", but instead of a heart he had "a membranous sac, or hollow viscus, cold and callous" [11]. In the *Travels* he suggests a method of putting a stop to duelling; if a man was killed in a duel both his body and that of his antagonist—who was to be hanged for murder—were to be given to the surgeons for dissection [12]. There is no allusion in Smollett which might suggest interest in the pathology of his time. Even tumours are very badly represented; for example, "a pernicious excrescence, which like an ulcerated tumour, exhausted the juices of the body by which it was fed" [13]; and "a cancerous ulcer through which all her blood and substance would be discharged" [14].

General surgery is also rather inadequately represented. Mr. Midshipman Crampley sustained "as pretty a luxation of the *os humeri* as one could wish to see" but we are not told the nature of the treatment [15]. Jack Rattlin is thrown from the rigging to the deck and sustains a compound fracture of the tibia. It is only the interference of Morgan and Random that prevents him from having the limb amputated—on the grounds that the resulting contusion, as Mackshane said, boded early mortification. The two mates having sawn off part of the splinter that stuck through the skin "reduced the fracture, dressed the wound, applied the eighteen-tailed bandage, and put the leg in a box, *secundum artem*". Cure was completed in six weeks [16]. In *Roderick Random*, the painter—Slyboot—is desirous of having a living model for a calvary, and he "believed it was possible for a man of a very nice hand, and exact knowledge of anatomy, to wound the diaphragma somewhere about the skirts, which might induce a singultus, without being attended with death" [17]. The York surgeon who proposed to take off Squire Burdock's scalp in order to ascertain whether the cranium was fractured is shown up in a very bad light. The operation, he says, might at any rate "be of service in giving vent to any blood that might be extravasated, either above or below the *dura mater*". "The operator, laying aside his coat and periwig, equipped himself with a night-cap, apron, and sleeves, while his 'prentice and footman, seizing the squire's head, began to place it in a proper posture." A description of the operation itself is spoiled by the sudden resuscitation of the

squire, who declares that "a man's skull is not to be bored every time his head is broken" [18]. Again in *Count Fathom* the surgeon suggests a trepan after the attorney receives a scalp wound [19]. It is interesting to note that Crabshaw in *Sir Launcelot Greaves* had been in the hands of surgeons for the treatment of a rupture: it is not to be wondered at that the treatment was not a success [20]. We might hope for some illuminating statement from Smollett regarding the treatment of hæmorrhoids in his day, but we come away from his works disappointed. He tells us only that St. Fiacre presides over blind piles; and that a female saint, Haemorrhöisa, comforts those distressed with bleeding piles [21].

Smollett frequently refers to the practice of phlebotomy, which was going slightly out of favour in his day. Certain possible opinions of Smollett emerge from his writings. The operation was often undertaken with the slightest of excuses. The chicken-hearted Strap, after a supposed wound, lies warm and breathing; without much inquiry regarding the nature of the damage, Roderick proposes to let blood—whereupon the barber immediately comes to life [22]. Roderick, incidentally, seems to have been rather an adept at the operation; he bled the gentleman of the sword after the latter had been bruised by a fall, and was paid half-a-crown for his services [23]. Squire Crabshaw had been bled three times by the apothecary [24], and the surgeon tells Captain Crowe, whose face is badly swollen from the use of his improvised helmet, that he must begin with a copious blood-letting and an emptying of the intestinal canal [25]. Peregrine Pickle's Swiss valet was able to perform phlebotomy on his master without delay while they were on the road, since he was always provided with a case of lancets [26]. Blood was usually drawn from the arm, but there is one reference to a bleeding from the veins of the foot [27], and another to a bleeding from the jugular [28]. The amount of blood drawn naturally varied, but many surgeons appear to have required special reasoning or inducements to make them deviate from the accustomed amount. Twelve ounces appears to be the amount which Smollett considered as the average, as was the case when Captain Gawky was bled [29]; but those persons who believed in bleeding as a fashionable operation for the treatment of minor grades of "ill humours" probably often had much less drawn—as was the case with Captain Whiffle [30]. Larger quantities were probably also taken; Crabshaw says of one practitioner: "He has not left so much blood in my body as would fatten a starved flea" [31]. Humphry Clinker used a horse-fleam and let blood in the farrier style [32]. In *Count Fathom* the death of a patient during the performance of phlebotomy is recorded [33].

(b) *Physiology and medicine*.—This group finds much better representation in the writings of Smollett. It is hardly to be expected at this early date that the physiological descriptions would be at all in the modern style; and such is the case. For example, the gentlemen of the regiment of Picardy did not suffer from chafing of the skin on the inside of their legs, a condition which troubled Random a great deal. But Roderick was plump, whereas the professional fighters were withered, so that their bodies could not have juice enough to supply a common issue [34]. Bramble in *Humphry Clinker* goes back to Galen for his observation that a barbel's roe is violently cathartic [35]. When he faints at the ball he is told that the attack was due to an "impression of fetid effluvia upon nerves of uncommon sensibility" [36]. In several other places the deleterious effects of foul smells are mentioned. Bramble also notes the interaction of body and mind. He says: "I find my spirits and my health affect each other reciprocally; that is to say, everything that discomposes my mind, produces a correspondent disorder in my body; and my bodily complaints are remarkably mitigated by those considerations that dissipate the clouds of mental chagrin" [37]. The germs, in fact, of modern psychotherapy. The courage which is born of fear is stated to be due to the agitation of the spirits into a state of fermentation (*Count Fathom*) [38].

Of purely medical conditions, dropsy is perhaps most frequently mentioned. At

the time of his grandfather's death Roderick was evidently too young to make a diagnosis, but the old gentleman showed a distemper which "mounted from his legs to his stomach"—surely a very picturesque, though inaccurate, description of dropsy [39]. Readers of the naval chapters of *Roderick Random* will scarcely forget the man "loaded with a monstrous ascites or dropsy" who was whipped up the mast [40]. Smollett does not omit the weakening of the arms, which ultimately failed and sent the man to his death. In *Humphry Clinker* the semi-quack, Dr. L——n, suggests to Bramble that he is suffering from dropsy, because his ankles are swelled, and because he appears to have the *facies leucophlegmatica* [41]. Bramble himself in a letter to his own physician, Dr. Lewis, says: "He told me the other day, with great confidence, that my case was dropsical; or, as he called it, *leucophlegmatic*; a sure sign that his want of experience is equal to his presumption; for, you know, there is nothing analogous to the dropsy in my disorder. I wish those impertinent fellows, with their rickety understandings, would keep their advice for those that ask it. Dropsy, indeed! Sure I have not lived to the age of fifty-five, and had such experience of my own disorder, and consulted you and other eminent physicians so often and so long, to be undeceived by such a —. But without all doubt the man is mad, and therefore what he says is of no consequence" [42]. The rich joke in the letter is in the postscript. It must be quite lost on lay readers. Bramble adds to his letter: "P.S.—I forgot to tell you that my right ankle pits: a symptom, as I take it, of its being *œdematous*, not *leucophlegmatic*." In *Peregrine Pickle*, Emilia's uncle was tapped for the dropsy and died within two days [43]. Over twenty years after Smollett wrote this Fothergill was suggesting that as few survived this operation its practice should be considerably reduced [44].

At the time when Smollett wrote, neurology was yet unborn, and it will not therefore be entirely unexpected if we find that his references to nervous cases relate mainly to apoplexy, epilepsy, and delirium. The deficiencies are those of the age and not of the man. An interesting point is that in those days a sudden shock or emotion might cause a loss of senses which persisted for weeks. Nor was this strange phenomenon peculiar to the fair sex. In fact, one might say facetiously that exactly the opposite was the case, for out of four examples taken at random, three of the patients were males, while only one was a female [45]. On the death of Roderick's mother, his father "was so affected with her death, that he remained six weeks deprived of his senses"; his "delirium was succeeded by a profound melancholy and reserve" [46]. In *Peregrine Pickle* a meeting of authors is taking place at a house when a cry of fire is raised. The chairman of the meeting jumps from the window on to a passing chair in which a beau was being carried. The latter was so much upset by the fright "that he was seized with a delirium, and lay a whole fortnight deprived of his senses; during which period he was not neglected in point of medicines, food, and attendance, but royally regaled, as appeared by the contents of his landlord's bill" [47]. No mention is made of the possible physical effect of a heavy man falling from a height on the head of another. In *Count Fathom* there is a good description of repeated hysterical fits which affected Miss Biddy [48]—and possibly to this cause we must ascribe most similar occurrences in the novels. Among the many penetrating descriptions of works of art which are found in the *Travels*, there is a short one of Raphael's *Transfiguration* [49]. It is interesting to note that Smollett makes no mention of the boy in the epileptic seizure who appears in the foreground of the picture. Mrs. Clewline in *Sir Launcelot Greaves* underwent a long series of hysterical fits and other complaints, which seemed to have a fatal effect on her brain as well as on her constitution; she became a habitual drinker [50]. Fainting is a much more common complaint than fits or delirium. Even the men are not exempt. Bramble faints at a ball [51], and later on he faints after phlebotomy [52]. The usual remedies were smelling salts and bathing of the temples with Hungary-water. Bramble on the second occasion presented a bad

case, and salt had to be laid under his head and body. He recovered in fifteen minutes.

In the realm of general medicine few illnesses are described fully. One of the most interesting is that of Crabshaw, the bullying squire of Sir Launcelot Greaves. Crabshaw had been beset by three persons with Venetian masks on their faces, and in the affray his "lower extremities were covered with blood, and all the rest of his body speckled with livid marks of contusion". He was placed in the hands of an apothecary, who later reported to Sir Launcelot that "he apprehended him to be in a very dangerous way from an inflammation of the *piamater*, which had produced a most furious delirium. Then he proceeded to explain, in technical terms, the method of cure he had followed; and concluded with telling him the poor squire's brain was so outrageously disordered, that he had rejected all administration, and just thrown a urinal in his face". Sir Launcelot then called in a very grave and sensible physician, who asked the apothecary about the symptoms. He was told "that the blood was seemingly viscous, and salt upon the tongue; the urine remarkably acrosaline, and the fæces atrabilious and fœtid. When the doctor said he would engage to find the same phenomena in every healthy man of the three kingdoms, the apothecary added, that the patient was manifestly comatous, and moreover afflicted with griping pains and borborygmata". When asked what had been done the apothecary replied "that venesection had been three times performed; that a vesicatory had been applied *inter scapulas*; that the patient had taken occasionally of a cathartic apozem, and between whiles, alexipharmic boluses and neutral draughts.—'Neutral, indeed,' said the doctor; 'so neutral, that I'll be crucified if ever they declare either for the patient or the disease.' So saying, he brushed into Crabshaw's chamber, followed by our adventurer, who was almost suffocated at his first entrance. The day was close; the window-shutters were fastened; a huge fire blazed in the chimney; thick harateen curtains were close drawn round the bed, where the wretched squire lay extended under an enormous load of blankets. The nurse, who had all the exterior of a bawd given to drink, sat stewing in this apartment like a damned soul in some infernal bagnio; but rising when the company entered, made her curtsies with great decorum.—'Well', said the doctor, 'how does your patient, nurse?'—'Blessed be God for it, I hope in a fair way. To be sure his apozem has had a blessed effect—five-and-twenty stools since three o'clock in the morning. But then, a'would not suffer the blisters to be put upon his thighs. Good lack! a'has been mortally obstropolous and out of his senses all this blessed day.'—'You lie,' cried the squire, 'I an't out of my seven senses, thof I'm half mad with vexation'" [53]. This is an extravaganza which is possibly not so very far removed from verity. No doubt Smollett intentionally praised the physician at the expense of the apothecary.

Strangely enough, hydrophobia is mentioned at least four times in Smollett's writings. The disease was at this time rare, and Heberden had never seen a case. One of Roderick Random's cronies is bitten on the cheek by a woman, and he is, though a doctor, apprehensive of the consequences of the bite, "for by this time he was convinced of her being mad" [54]. One member of the company prescribed the actual cautery, and another suggested that the part should be scooped out with the point of his sword. In *Peregrine Pickle* much rough fun is abstracted from the misfortune of Pallet, who is suspected to be suffering from hydrophobia, and one of the characters is made to say that the disease sometimes appears in persons not previously bitten by a mad dog [55]. In *Humphry Clinker* expression is given to a popular notion that if a dog went mad, persons who had been bitten by it before the onset of its madness would also be infected [56]. In the *Atom* we read of "the vulgar conceit that the liver of a mad dog being eaten is a preventive against madness" [57].

In various places we find reference to rickets and to scurvy. An interesting one is in a letter from Jack Melford in *Humphry Clinker*. He says that the turnips of

Scotland are superior to those of England: "They are small and conical, of a yellowish colour, with a very thin skin; and, over and above their agreeable taste, are valuable for their antiscorbutic quality" [58]. Gout is mentioned quite frequently.

(c) *Infectious diseases*.—Smollett's knowledge of the cause of infectious diseases was that of his time, but in his works we find occasional references to even older beliefs. He is certainly being farcical when he makes Crabshaw say that "cowardice and madness are both distempers, and differ no more than the hot and cold fits of an ague" [59]. Perhaps he was more in earnest when he tells us that Sir Everhard Greaves suffered disagreeable tidings, and that this, together with a severe fit of the gout, and gravel, produced a fever [60]. He was nearer the ideas of his time when he makes Mr. Tomlins, who had been confined to his cabin on board ship, die of a severe fever, which was due to want of air [61]. More interesting is Matt. Bramble's letter from Bath. He says: "The very air we breathe is loaded with contagion. We cannot even sleep without risk of infection. I say, infection. This place is the rendezvous of the diseased. You won't deny that many diseases are infectious; even the consumption itself is highly infectious" [62]. He then goes on to point out the risk of infection from bed-clothing—a subject which also receives his attention in the *Travels*. Of London he says: "I breathe the steams of endless putrefaction; and these would, undoubtedly, produce a pestilence, if they were not qualified by the gross acid of sea-coal, which is itself a pernicious nuisance to lungs of any delicacy of texture" [63].

In *Roderick Random* there is an interesting description of an epidemic fever which wrought havoc in the fleet. "The change of the atmosphere . . . conspired, with the stench that surrounded us, the heat of the climate, our own constitutions impoverished by bad provisions, and our despair, to introduce the bilious fever among us, which raged with such violence, that three-fourths of those whom it invaded died in a deplorable manner; the colour of their skin being, by the extreme putrefaction of the juices, changed into that of soot" [64]. His own illness is well described, and it is possible that this disease may have been yellow fever. That it was possibly not typhus is shown by the fact that this disease broke out later among the slaves "and carried off a good many of the ship's company"; yet this outbreak is mentioned merely as an exception to the statement that they had met with "nothing remarkable" on the voyage. Although there was a "Black Assize" in London in 1750, the only other reference to typhus occurs in *Count Fathom*, which was published in 1753. Ferdinand, after a forced retirement, returns to court, but his former acquaintances "avoided him accordingly as the gaol infection" [65].

Smallpox is not as frequently mentioned as one would expect. Several persons are described as being pock-marked, and the death of Tommy Clewline from this "loathsome, pestilential malady" is described [66]. Smollett was possibly impressed by the frequency of the disease in his native Scotland, since he makes Bramble say in a letter that "this air, however, notwithstanding its humidity, is so healthy, that the natives are scarce ever visited by any other disease than the small-pox, and certain cutaneous evils" [67]. Jack Melford describes how the Highlanders regale themselves on whisky, which they swallow in great quantities "without any sign of inebriation. They are used to it from the cradle, and find it an excellent preservative against the winter cold, which must be extreme on these mountains. I am told that it is given with great success to infants as a cordial in the confluent small-pox, when the eruption seems to flag, and the symptoms grow unfavourable" [68].

Consumption receives considerable attention in the writings of Smollett—mainly in the *Travels* and in his letters. There is no evidence that he held views which were at all remarkable. His consultation with Professor Fizes, "the Boerhaave of Montpellier", regarding his own chest complaint is of some interest, in that it shows how dogmatic Smollett could be on these matters [69].

Venereal disease is mentioned on at least ten occasions. A number of these references describe the results of syphilis, graphically, yet not in a manner which indicates that Smollett had anything unusual to say on the subject. It is evident that syphilis was at that time a favourite disease for the exercise of quackery. For further information on this subject reference should be made to the paper by Rolleston [70].

Time does not permit me to deal with the many observations which Smollett passed on the *materia medica* of his day. I must also pass over his comments on insanity, and his description of the private asylum in *Sir Launcelot Greaves* [71]; his numerous references to airs and places, and his criticism of the hygiene and sanitation of the time—found abundantly not only in the novels, but also in the *Travels* and in the *Letters*. His trenchant description of abuses in the Navy, which appears in *Roderick Random*, is well known, and it has already been adequately dealt with by Drinker [5]. Before closing I should like to deal, however, with his reflections on those who practised medicine and its allied crafts.

In Smollett's day medical men were divided into the three classes of apothecaries, surgeons, and physicians. Lowest in the scale were the apothecaries. Some rung up the ladder were the surgeons—still not completely emancipated from the stigma of the brush and razor. Highest of all were the physicians. If we are to believe Smollett, combination between the three classes seems to have been very common. For example, concerning Peregrine's sojourn in Bath he says: "He perceived, that, among the secret agents of scandal, none were so busy as the physicians, a class of animals who live in this place, like so many ravens hovering about a carcass, and even ply for employment, like scullers at Hungerford Stairs. The greatest part of them have correspondents in London, who make it their business to inquire into the history, character and distemper of everyone that repairs to Bath, for the benefit of the waters, and if they cannot procure interest to recommend their medical friends to these patients before they set out, they at least furnish them with a previous account of what they could collect, that their correspondents may use this intelligence for their own advantage. By these means, and the assistance of flattery and assurance, they often insinuate themselves into the acquaintance of strangers, and by consulting their dispositions, become necessary and subservient to their prevailing passions. By their connection with apothecaries and nurses, they are informed of all the private occurrences in each family, and therefore enabled to gratify the rancour of malice, amuse the spleen of peevish indisposition, and entertain the eagerness of impertinent curiosity" [72]. In his description of the attempt of the pseudo-doctor Fathom to set up a practice in London, he says: "In his researches he found that the great world was wholly engrossed by a few practitioners who had arrived at the summit of reputation, consequently were no longer obliged to cultivate those arts by which they rose; and that the rest of the business was parcelled out into small enclosures, occupied by different groups of personages, male and female, who stood in rings and tossed the ball from one to another, there being in each department two sets, the individuals of which relieved one another occasionally. Every knot was composed of a waiting-woman, nurse, apothecary, surgeon and physician, and sometimes a midwife was admitted into the party" [73].

Smollett's opinion of the apothecary was evidently low. In the *Atom* a character is made to say: "My Lord Cuboy, your grace talks like an apothecary" [74]. Roderick says of Mr. Lavement, his apothecary-employer: "His expense for medicines was not great, for he was the most expert man at a succedaneum of any apothecary in London; so that I have been sometimes amazed to see him, without the least hesitation, make up a physician's prescription, though he had not in his shop one medicine mentioned in it. Oyster shells he could invent into crab's eyes; common oil into oil of sweet almonds; syrup of sugar, into balsamic syrup; Thames water into aqua cinnamoni, turpentine into capivi; and a hundred more costly

preparations were produced in an instant, from the cheapest and coarsest drugs of the *materia medica*: and when any common thing was ordered for a patient, he always took care to disguise it in colour or taste, or both, in such a manner as that it could not possibly be known" [75]. The description of the quack, Ferret, selling drugs, which is found in *Sir Launcelot Greaves*, is good farce; but in addition, it is probably based on fact [76].

The surgeons are depicted in a less sordid atmosphere, but Smollett was evidently impressed by their jealousy of the physicians and of each other. When Roderick was being interviewed by Mr. Crab, the surgeon, he informed the latter that he had studied the art with great pleasure and application. "'Oho! you did?' says Crab. 'Gentlemen, here is a complete artist!—studied surgery! What? in books, I suppose. I shall have you disputing with me one of these days on points of my profession. You can already account for muscular motion (I warrant) and explain the mystery of the brain and nerves—ha? You are too learned for me, damn me. But let's hear no more of this stuff. Can you bleed and give a clyster, spread a plaster, and prepare a potion?' " [77]

Even when dealing with the physicians Smollett is hardly less scathing. In *Peregrine Pickle* a character says ironically: "Egad! I believe he's a physician." To which Peregrine replies, "Sir, a physician may be a man of honour" [78]. Even the members of this highest class of the profession were not exonerated from the charge of keeping their patients lingering on and on, in order that the bill might run up and up. To quote from *Peregrine Pickle* again: "His noble patron was seized with an apoplectic fit from which he was recovered by the physicians, that they might despatch him according to rule; and in two months after they were called, he went the way of all flesh" [79]. The voice of the satirist is heard again in *Count Fathom*: "When a physician becomes the town talk, he generally concludes his business more than half done, even though his fame should wholly turn upon his mal-practice; insomuch that some members of the faculty have been heard to complain, that they never had the good fortune to be publicly accused of homicide; and it is well known that a certain famous empiric, of our day, never flourished to any degree of wealth and reputation till after he had been attacked in print, and fairly convicted of having destroyed a good number of the human species" [80].

Well, is this the farcical romancer talking, or is it the voice of the satirist, who in *Roderick Random*, wrote passages which had admittedly much influence on the development of better conditions in the Navy in later years? I venture to suggest that, while Smollett was depending upon "rollicking farce" to produce his effects, the voice of the satirist was also speaking. It was admitted by those who knew him that he had not the type of imagination which could create, say, a *Tom Jones*, and that when he wrote he did so from his own experience and observation. Despite the many hard things which he said about his profession, he retained the friendship and esteem of numerous doctors well known in his day and since, foremost among whom were the Hunters. He was writing to both the brothers almost up to the time of his death. Quarrels he certainly had with other doctors—for example, Mark Akenside—but few men in Smollett's circle could have been immune to his ill-humour. To me the fact that many of his friends were the foremost medical men of his time, and that he kept their friendship so long, suggests that the bludgeons of his satire were finding their mark. Men such as the Hunters were quite capable of realizing the weak points of the medicine of their day, and it is hardly likely that they would have continued on terms of intimacy with Smollett if they had thought that his criticisms of their professional brethren were unjust.

From this brief review it will, I think, be apparent that Smollett's comments on the medicine of his day, while they are usually amusing and often very apt, show little evidence that he was interested in the development of medical science. Like many others in his age, he was content to use the language of the ancients. It would

seem that Smollett was quite a sound practitioner, and that his comparative failure in medicine was due to his temperament rather than to his methods. It is only when he is writing about matters and conditions which touched him closely as an individual that we feel that the thought in his mind is about what might be, rather than about what is, or was. At these times he becomes, in medical or social questions, the reformer and not the scientist.

He was obviously a keen observer, and he set down in spirited prose the facts as he saw them. In later years these facts were often of a scientific nature, especially in the *Travels*. But the facts as Smollett saw them were sometimes coloured by his own temperament. One could imagine him writing an excellent description of a patient's symptoms but one could also visualize him in consultation about a patient—a dogmatic and somewhat irritable colleague.

As a man of letters his fame has been somewhat obscured by the attitude of earlier critics; but, as Seccombe [81] remarks, he was the first great man of letters to make his living entirely out of his literary work—without help from patrons or others. Although he owes little to the scientific work of his day, it is pleasing to think that his training and early experience in medicine may have played their part in developing his faculty for accurate observation and graphic description—the essential backbone of his prose.

REFERENCES

- 1 TREVELYAN, G. M., *History of England*, London, 1926, p. 506.
- 2 *Humphry Clinker*, Letter from Bath, April 28 (to Dr. Lewis).
- 3 *Ibid.*
- 3a Letters, edited by E. S. Noyes, Harvard, 1926, p. 101.
- 4 *Peregrine Pickle*, Chap. lxxxi, *Memoirs of a Lady of Quality*.
- 5 DRINKER, C. K., *Ann. M. Hist.*, 1925, 7, 31.
- 6 BECK, C., *Am. J. Surg.*, 1936, 32, 383.
- 7 JONES, C. E., *Bull. Inst. Hist. Med., Johns Hopkins*, 1935, 3, 31.
- 8 *Roderick Random*, Chap. xviii.
- 9 *History and Adventures of an Atom*, edit. Hutchinson & Co., p. 256.
- 10 *Ibid.*, p. 268.
- 11 *Ibid.*, p. 320.
- 12 *Travels through France and Italy*, Letter xv.
- 13 *History and Adventures of an Atom*, edit. Hutchinson & Co., p. 316.
- 14 *Ibid.*, p. 372.
- 15 *Roderick Random*, Chap. xxvii.
- 16 *Ibid.*, Chap. xxviii.
- 17 *Ibid.*, Chap. xli.
- 18 *Humphry Clinker*, Letter from Harrowgate, June 26 (to Dr. Lewis).
- 19 *Count Fathom*, Chap. xxxviii.
- 20 *Sir Launcelot Greaves*, Chap. iv.
- 21 *History and Adventures of an Atom*, edit. Hutchinson & Co., p. 377.
- 22 *Roderick Random*, Chap. ix.
- 23 *Ibid.*
- 24 *Sir Launcelot Greaves*, Chap. xvi.
- 25 *Ibid.*, Chap. xvii.
- 26 *Peregrine Pickle*, Chap. lxxviii.
- 27 *Roderick Random*, Chap. lxi.
- 28 *Ibid.*, Chap. xxvii.
- 29 *Ibid.*, Chap. xxi.
- 30 *Ibid.*, Chap. xxxv.
- 31 *Sir Launcelot Greaves*, Chap. ii.
- 32 *Humphry Clinker*, Undated letter (? Oct. 5) from J. Melford to Sir Watkin Phillips, Bart.
- 33 *Count Fathom*, Chap. liv.
- 34 *Roderick Random*, Chap. xliii.
- 35 *Humphry Clinker*, Introduction, to Mr. Henry Davis.
- 36 *Ibid.*, Letter from Bath, May 8 (to Dr. Lewis).
- 37 *Ibid.*, Letter from London, June 14 (to Dr. Lewis).
- 38 *Count Fathom*, Chap. xxi.
- 39 *Roderick Random*, Chap. iv.
- 40 *Ibid.*, Chap. xxvii.
- 41 *Humphry Clinker*, Letter from Hot Well, Bristol, April 18 (to Sir Watkin Phillips).
- 42 *Ibid.*, Letter from Hot Well, Bristol, April 20 (to Dr. Lewis).
- 43 *Peregrine Pickle*, Chap. ciii.
- 44 FOTHERGILL, J., *Works*, 1782, 2, 85.
- 45 *Peregrine Pickle*, Chap. xciv. Also *vide* refs. (46), (47), (48).
- 46 *Roderick Random*, Chap. i.

- 47 *Peregrine Pickle*, Chap. xciv
- 48 *Count Fathom*, Chap. li.
- 49 *Travels through France and Italy*, Letter xxxiii.
- 50 *Sir Launcelot Greaves*, Chap. xxi.
- 51 *Vide ref.* (36).
- 52 *Vide ref.* (32).
- 53 *Sir Launcelot Greaves*, Chap. xvi.
- 54 *Roderick Random*, Chap. xlvi.
- 55 *Peregrine Pickle*, Chap. lvii.
- 56 *Humphry Clinker*, Letter from London, May 24 (to Sir Watkin Phillips).
- 57 *History and Adventures of an Atom*, edit. Hutchinson and Co., p. 280.
- 58 *Humphry Clinker*, Letter from Edinburgh, August 8 (to Sir Watkin Phillips).
- 59 *Sir Launcelot Greaves*, Chap. viii.
- 60 *Ibid.*, Chap. iv.
- 61 *Roderick Random*, Chap. xxxvii.
- 62 *Humphry Clinker*, Letter from Bath, April 28 (to Dr. Lewis).
- 63 *Ibid.*, Letter from London, June 8 (to Dr. Lewis).
- 64 *Roderick Random*, Chap. xxxiv.
- 65 *Count Fathom*, Chap. lv.
- 66 *Sir Launcelot Greaves*, Chap. xxi.
- 67 *Humphry Clinker*, Letter from Cameron, September 6 (to Dr. Lewis).
- 68 *Ibid.*, Letter from Argyleshire, September 3 (to Sir Watkin Phillips).
- 69 *Travels through France and Italy*, Letter xi.
- 70 ROLLESTON, J. D., *Brit. J. Ven. Dis.*, 1934, **10**, 147.
- 71 *Sir Launcelot Greaves*, Chap. xxiii.
- 72 *Peregrine Pickle*, Chap. lxx.
- 73 *Count Fathom*, Chap. lii.
- 74 *History and Adventures of an Atom*, edit. Hutchinson and Co., p. 317.
- 75 *Roderick Random*, Chap. xix.
- 76 *Sir Launcelot Greaves*, Chap. x.
- 77 *Roderick Random*, Chap. vii.
- 78 *Peregrine Pickle*, Chap. xl.
- 79 *Ibid.*, Chap. xcii.
- 80 *Count Fathom*, Chap. liii.
- 81 SECCOMBE, T., introduction to Smollett's "Travels", edit. World's Classics, 1907.

Section of Dermatology

President—H. W. BARBER, M.B., F.R.C.P.

[March 18, 1937]

Changes in the Pilosebaceous Follicles and Sebaceous Secretion following Herpes Zoster.—H. W. BARBER, M.B.

A. P. This case is the fourth in a series that I have met with during the past two years.

The first was that of a middle-aged man who originally consulted me on account of dermatitis herpetiformis, from which he recovered, and later on account of psoriasis. In September 1934 he had a very severe attack of right-sided supra-orbital herpes zoster, with involvement of the eye. I did not see him during this attack, but he came to me about six weeks later, when I noted that over the area on the right side of the scalp which had been affected by the zoster, the pilosebaceous follicles were plugged with comedo-like concretions. I had not previously observed this as a sequel to herpes zoster, and I ascribed it to paralysis of the pilomotor muscles, due to involvement of their sympathetic nerve-supply, with consequent retention of sebum in the infundibula of the follicles and subsequent comedo-formation. Although it is generally admitted that contraction of the pilomotor muscles plays some part in the expulsion of sebum, I now believe this explanation to be wrong.

My second case was in a woman with anorexia nervosa, who originally consulted me on account of stomatitis caused by taking large doses of calomel over a long period. She came to me again in January of this year owing to an exactly similar plugging of the pilosebaceous follicles around the upper part of the left chest, corresponding to the area involved by an attack of herpes zoster which she had had in October last.

My third case was in a man whom I had treated in 1933 for eczema. He consulted me again in January of this year because of a slight return of his eczema. He had had an attack of herpes zoster, involving chiefly the right shoulder, several weeks previously, and again the same plugging of the follicles was observed. Dr. Forman saw him with me, and we removed several of the comedo-like bodies for microscopical examination, which revealed that they were structurally comedones, but contained no acne bacilli.

The patient I am showing to-day is a man aged 64, who was sent to me for treatment of psoriasis. In October 1936 he had had a severe attack of left supra-orbital zoster, which lasted about three weeks. He noticed the comedo-formation towards the end of December.

Over the part of the scalp affected by the herpes are seen numerous irregular scars, interspersed between areas of non-scarred skin. On the latter are seen grouped yellowish points, which are presumably dilated sebaceous glands. Their appearance recalls that of the so-called "Fordyce's disease of the lips". They are particularly well seen on the left temple where there is no scarring. There is also present the comedo-formation in the infundibula of some of the follicles observed in my other cases.

Dr. R. T. Grant investigated the patient for me and reported as follows:—

"There is clear evidence of interference with the nervous supply over the affected regions of the scalp. Over the scarred area there is definite hypæsthesia and patches of anaesthesia, to cotton-wool, to pin-pricks, and to faradism. Faradism does not produce goose skin on either side of the forehead. The temperatures of the two sides of the forehead are equal, but on warming the body by immersing the legs in water, there is much more sweating over the normal than over the affected side. For the moment, however, I do not know whether to attribute the reduction of sensation and sweating to injury of the sensory and sympathetic nerve trunks or to the inflammatory process in the skin which has produced the scarring.

With such an inflammatory process one can conceive an interference to glandular secretion arising not only by paralysis of the secretory nerves, but also by injury to the glands themselves."

With regard to Dr. Grant's observations, it is clear that the groups of what I take to be dilated sebaceous glands, and the majority of the comedones, occur where there is no scarring and where the skin has not apparently been altered by the inflammatory process. I think therefore that one can legitimately ascribe the changes in the sebaceous glands, and indirectly in the follicles, to involvement of the nerve-supply of the glands. That the secretion of sebum is under the control of the sympathetic nervous system is generally recognized.

It may be added that in none of these cases had any local application been used which could produce comedo formation.

Discussion.—Dr. F. PARKES WEBER asked if the President regarded the changes in question as secondary to nervous lesions. He had seen a trophic change of one upper limb, following herpes zoster, apparently due to lesions in the autonomic nervous system.

The PRESIDENT (in reply) said that, judging from the present case, he presumed that the sympathetic nerve-fibres which controlled sebaceous secretion had been paralysed by the herpes zoster. He had seen the patient in his first case since he had observed the changes in the follicles and, apart from the scarring, the skin was now normal. In the present case the pilosebaceous plugs were fewer than they were some weeks ago, and the apparent dilatation of the sebaceous glands was less. He thought that the only explanation was an involvement of the sympathetic fibres supplying the sebaceous glands.

Necrobiosis Lipoidica Diabeticorum.—ROBERT KLABER, M.D.

This patient was shown at a meeting of the Section in 1933.¹ Sections then obtained showed necrobiotic foci, surrounded by foam cells and new capillaries. Frozen sections indicated that these necrobiotic areas stained diffusely with Scharlach R, and, by means of a polarizing microscope, a few doubly refracting crystals, believed to be cholesterol esters, were demonstrated in the centre of these lipid foci. An occasional histiocyte, loaded with lipid granules, could be observed.

This case differed from those previously described in the finding of cholesterol crystals. It has since differed also from the majority reported in the immediate response of the skin lesions to control of the diabetes by Dr. George Graham, after being previously active for three years. It may be worth noting that some improvement followed a simple reduction of fat intake, before the carbohydrate metabolism was seriously tackled.

The blood-sugar has since been maintained at a normal level by the administration of 8 to 10 units of insulin daily. In the meanwhile, the lesions have involuted until all except one now show only atrophic scars. One scar only, on the right ankle, shows some hypertrophy and discoloration, with overlying telangiectases.

This case, therefore, while clinically showing the classical features of Urbach-Oppenheim's disease, both in its histology and response to treatment suggests the close relation of this condition to xanthoma diabeticorum. It seems possible that the same factors, with the addition of varying degrees of focal infarction, are responsible for necrobiosis lipoidica diabeticorum.

Sebocystomatosis (Günther).—ROBERT KLABER, M.D.

This woman, aged 36, has been attending hospital for some time on account of a persistent erythematous squamous eruption on the face. The appearances of this eruption vary greatly from time to time, usually resembling seborrhœic eczema or rosacea, but sometimes being more suggestive of lupus erythematosus, and at other times even suggesting a rosaceous tuberculide. The condition has proved extremely

¹ *Proceedings*, 1933, 27, 713 (Sect. Derm., 31)

resistant to a great variety of local and other treatments. She is now having gold injections.

Of no interest to the patient is the presence of a score of small cysts in the skin overlying the epigastrium. These cysts have been present as long as she can remember. Their size varies from that of a small to a large pea; their colour from yellow to grey. On the surface of some may be seen a single, dilated, blocked follicle. These somewhat enlarged blocked follicles are also conspicuous below the cysts, especially in the suprapubic scars, resulting from operations for hernia and ovarian cyst.

I think it will be agreed that the clinical appearances are typical of the rare condition first described by Pringle as "steatocystoma multiplex" and subsequently by Günther as "sebocystomatosis".

The study of serial sections following excision of these small cysts, shows several striking features:—

- (1) Small follicular horny cysts at various levels in the epidermis and dermis;
- (2) The two large cysts, originally quite spherical on excision, have been shrunken by dehydration;
- (3) One of the cysts is seen to contain a whorled mass of lanugo hairs; and
- (4) A sebaceous gland lying on the wall of this cyst is seen to communicate directly with its lumen.

These histological appearances support the view that this condition is a cystic naevus of pilosebaceous origin.

At the meeting last October Dr. Parkes Weber showed two brothers having this condition, and in addition appearing to have what would otherwise have been regarded as sebaceous cysts; the question arises whether this condition, in its origin and histology, bears any relation to those sebaceous cysts.

Discussion.—Dr. F. PARKES WEBER, in reply to Dr. Klaber's question concerning the two brothers whom he (Dr. Weber) had shown at a meeting of the Section,¹ said that no histological examinations had been made, but since then he had seen a young woman who had sebocystomatosis, localized especially in both axillae. In that case a biopsy had been made, and Dr. Freudenthal would be able to answer Dr. Klaber's question about it, i.e. as to the origin of the cysts. He (Dr. Weber) preferred the term "sebocystomatosis", just as he preferred "xanthomatosis" to "xanthoma multiplex".

Dr. W. FREUDENTHAL said that sections obtained from Dr. Parkes Weber's recent case showed cysts of the sebaceous glands and of the hair follicles. The former were attributed to obstruction of sebaceous ducts; the latter to obstruction of hair-ostia. The apocrine glands were normal. In Dr. Klaber's case, the presence of comedones overlying the cysts and in the suprapubic scars raised the question as to whether these cysts might not be pilosebaceous retention cysts.

Dr. I. MUENDE said that he first saw a case of sebocystomatosis, in Vienna, eight years ago when the patient, a man, had numerous lesions distributed over the midline of the chest and also the axillae. He cut serial sections as he then had the idea that the cysts might possibly have arisen from the apocrine glands. The histological study, however, did not confirm any such association and he accepted the view that the cysts arose as a result of blockage of the pilosebaceous follicle. Although in the four cases shown in England the patients were women, Günther's 18 cases were in men, and statistics appeared to show that it was more common in men than in women. This feature was, he thought, one which did not lend support to the contention that it was due to an association with the apocines.

POSTSCRIPT (25.5.37).—Small axillary cysts are now developing. [R.K.]

Lichen Sclerosus et Atrophicus (Hallopeau).—ROBERT KLABER, M.D.

The patient is a woman aged 53. The condition began seven years ago when her daughter noticed a white patch in the small of her back. Since then, further similar lesions have appeared over many areas. The appearance of a new patch is not

¹ Weber, F. P., and Schlüter, A., *Proc. Roy. Soc. Med.*, 1936, **30**, 29 (Sect. Derm., 7).

associated with any pain or irritation, but is usually preceded by a week's general malaise. The lesions are white from the beginning.

Condition on examination.—The patient is a short, obese woman, of Russian extraction. There is a small xanthelasma on the left upper lid.

Situation of lesions.—Sternum and infra-mammary region (fig. 1); lateral chest and abdominal wall (on the left side, there is a scleroderma-like band with two advancing pseudo-pods); middle and lower back and sacral region (fig. 2); front of wrists; none on the mouth or scalp.

The primary lesions vary in size from 2 mm. to 2 cm. They consist of very hard white scleroderma-like spots or plaques in which plugged patulous follicles may be recognized. Later, these plugs fall out. The margin is at first often violaceous, as in morphœa, and then well-marked brown pigmentation appears; partial involution of many lesions then occurs, leaving mottled brown and white less dense plaques.



FIG. 1.—Guttate lesions on chest and upper abdomen and superficial ulceration of plaques under breast.

The sacral lesions have, on two occasions, suddenly become painful, owing to a bullous change in the whole lesion. No history of trauma could be obtained on either occasion.

The lesions below the very large breasts have resulted in secondary painful ulceration. This pain has been reduced and healing has followed quarter-pastille doses of X-rays. The patient has, however, now had eight exposures and ulcers continue to form.

X-rays have not appeared to be of any benefit on the non-ulcerated areas.

The blood calcium is 11.8 mgm. %. Treatment by ammonium chloride did not appear to help. Special brassières have been ordered.

Histology of sections demonstrated.—The epithelium shows well-marked hyperkeratosis. The hair follicles are widely dilated and filled with keratinous masses which in one area has led to the formation of a keratinous cyst. The other epithelial layers show variations in thickness. The upper part of the corium shows greatly dilated lymphatics associated with a high degree of œdema, which in some areas



FIG. 2.—Sacral region. Uppermost lesion is in bullous phase.

suggests an early, deep, bullous formation. Van Gieson's staining shows only a few irregular small patches of scleroderma-like amorphous condensations.

A section of an old lesion from the trunk shows well-marked epithelial atrophy.

Discussion.—Dr. FREUDENTHAL said there was a controversy whether lichen sclerosus was a special form of lichen planus, a disease *sui generis* (Miescher), or a variety of scleroderma. His own view was that lichen sclerosus, in spite of its peculiar clinical and histological features, should be considered as a member of the scleroderma family. This opinion was supported by the present case which showed, in addition to typical lichen sclerosus lesions, a band-like scleroderma. This must be something more than coincidence.

Dr. F. PARKES WEBER asked how Dr. Klaber accounted for the scleroderma-like thickening of the skin of part of the abdomen.

Dr. KLABER (in reply) said he agreed that the present appearances of some areas, especially the band on the left side, were indistinguishable from those of scleroderma. The bullous change which could be observed in the sacral region, and had been demonstrated in sections, and the marked plugging of follicles in the early stages, were not a part of ordinary scleroderma. He inclined to the view that this condition was neither lichen planus nor scleroderma, but probably a disease *sui generis*, which led to a secondary scleroderma.

Recurrent Ulceration of Mouth.—ELIZABETH HUNT, M.D.

L. C., a married woman, aged 38, has suffered from recurrent ulcers in the mouth for a year, and from a rash on the forearms and lower part of the legs for the same time.

In the mouth, lesions of different types have been observed; on the tongue, ulcers at the sides and underneath; on the upper surface, whitish plaques in one place, and in another a glazed patch denuded of papillæ with a circumscribed whitish border. Ulcers have also formed on the mucous membrane of the cheeks and on the gums.

The lesions appear in little groups and are raised and become bullous: later the bullæ coalesce to form shallow crateriform ulcers which are very painful and prevent

the wearing of dentures. Cultures from the ulcers gave a hæmolytic long-chain streptococcus approximating to *S. pyogenes* in cultural character.

On the legs and arms the rash shows scattered nummular lesions, in some places resembling psoriasis, but there is no dilatation of the papillæ on grattage. Others show a very slight scaling and seem formed of closely-set red, shiny, flat-topped papules. Some spots look hæmorrhagic but show no coloration or only a very pale coloration on diascopy. The lesions are very persistent—a few only have resolved, leaving pale brown pigmentation. Subjective symptoms are slight.

Occasional bullæ have also appeared on the skin, on a bright red base, which were painful and accompanied at onset by irritation. On the backs of the hands are a few lesions resembling erythema iris, and on the right hand is an ulcerated lesion; I am not sure whether this began as a bulla or as a chilblain. Bullous lesions have also appeared on the feet, the heels, and toes.

The patient is healthy and well developed, and has had three children. Blood picture normal. Wassermann reaction negative.

An autogenous vaccine was given and improved the condition of the mouth temporarily.

From the appearance of the mouth I thought this might be a case of bullous lichen planus and that the streptococcal infection was secondary. The skin lesions are not clinically typical lichen planus, but suggest rather the polymorphous lesions of erythema multiforme.

Dr. KNOWSLEY SIBLEY, referring to the lesions in the mouth, said that about forty years ago (*Brit. M. J.*, 1899 (i), p. 900) he showed a case of what he described as stomatitis neurotica chronica; he considered the present case an instance of that condition. The cases occurred in women, and the lesions occurred in various parts of the mouth, on the buccal mucosa, the tongue and the lips. They were very persistent, continuing for years, and nothing seemed to benefit them. All the patients were of the neurotic type. The present patient said that these ulcers had developed after she had had some special worry. The case he had a long time ago was that of a society lady, who had the condition on and off for twenty years, and sometimes the lesions were so bad that she shut herself up for weeks and refused to see anybody. She also attributed the condition to worry. He had had similar cases in recent years, but in none of those which he had seen had there been these lesions on the skin. The ulcers were fairly deep, and often very painful, and resistant to treatment.

Rhythmical Neutropenia with Recurrent Buccal Ulceration.—DENNIS EMBLETON, M.B.

On November 6, 1936 the patient, a married woman aged 43, had small ulcers in the mouth, accompanied by some malaise. Several similar attacks had occurred previously. Her health was perfect, except when the ulcers were present, then she experienced malaise, temperature from 99° to 100° F. (on one occasion 101° F.); some enlargement of the submental glands.

Past history.—Attacks of recurrent buccal ulceration, similar to the present attacks, occurred between 1919 and 1926, after a period of poor health, on each occasion lasting for some months. No amidopyrine or other drug had been taken previous to October 1936.

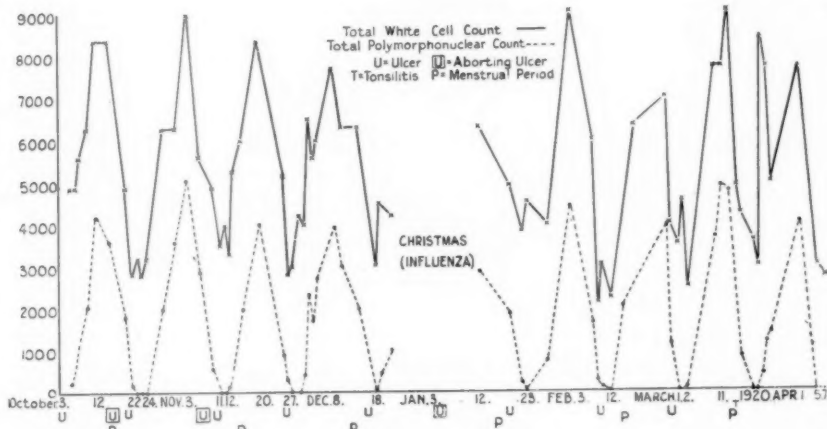
The present series of ulcers appears to have begun following an attack of influenza on July 25, 1936. Seventeen days later—on August 11—there was an attack of tonsillitis, but no ulceration of the mouth was noticed. On August 29—eighteen days subsequently—ulcers in the mouth began. The next crop occurred on September 15, after an interval of seventeen days. During this attack the first blood-count was taken and a marked neutropenia was noted. Subsequent observations showed that the ulcers usually occurred during the drop in neutrophils, generally a day or two before the lowest count was obtained. Ulcers have frequently been preceded by what is referred to as an aborting ulcer, the aborting ulcer generally corresponding to the earliest evidence of a fall in the blood-count.

The ulcers, therefore, showed a rhythmical incidence of from seventeen to nineteen days.

Agranulocytic periods occurred probably on October 5, October 22 (seventeen days), November 11 (twenty days), November 30 (nineteen days), December 18 (eighteen days). On December 28 a violent cold began, and no observations were possible. No ulcer occurred, but there was an aborting ulcer on January 3, on the tongue. The next agranulocytic period occurred on January 23, which was thirty-six days—or two eighteen-day periods—since the December attack. The subsequent agranulocytic periods have occurred on February 12 (twenty days), March 1 (seventeen days), when it was followed by an attack of tonsillitis and a sloughing area was noticed on the right tonsil and on the tip of the tongue.

Ulcers have appeared with each agranulocytic period, except at Christmas, following the cold. They are preceded by a burning, pricking sensation; this often occurs without the actual formation of an ulcer. The sensation has also occurred at intervals between 1926 and the present time, occasionally being followed during this period by a full ulcer.

The ulcers are situated on the lip, cheek, or tongue, never on the gums; once or twice they have been on the throat. When first noticed, they appear as a small



raised red area which may clear up or increase in size, ultimately developing into an ulcer with reddish margins containing a slough. The ulcers may vary in size from a pin's head to a lesion half an inch in length. The slough subsequently separates in three to five days, leaving a raw area which is exceedingly tender when touched. Healing occurs in from a week to ten days.

There is generally an enlargement of the submental glands with the development of the ulcers. No Vincent's organisms, moulds, yeasts, or hæmolytic streptococci have been found. The drop in the white cells is not the only disturbance in the blood picture; there is a coincident drop in the red cells, often of a million, with the appearance of marked vacuolation and aniso- and poikilo-cytosis. At the period of depression there is, as a rule, a marked increase in the platelets.

Treatment.—The patient has been hypervitaminized and treated with iron. Enormous quantities of liver have been injected and taken by the mouth. Recently pento-nucleotide has been injected daily. The treatment has apparently in no way influenced the rise and fall of the cells.

There is no relationship between the swing of this rhythm and the menstrual periods, as has been usually described in other rhythmical cases. A somewhat similar case was seen in the summer of 1936 which had been reported in the American papers, with a twenty-one day rhythm, but the blood picture differed to some extent.

Summary.—The peculiarities of this case appear to be :—

- (1) The extraordinary regular rhythm in the rise and fall of the leucocyte count.
- (2) The accompanying variation in the total number of red cells—a rise and fall of a million.
- (3) The marked increase in platelets at the period of maximum depression.
- (4) The development of the ulcers before the complete drop in the leucocyte count.
- (5) The remarkable good health enjoyed by the patient throughout the period of observation. She appears to be in perfect health, but actually has less than 1% polymorphonuclear leucocytes in the blood.

[Dr. Embleton demonstrated a second case of recurrent ulceration on the tongue, in which a drop of over a million red cells had occurred in two days, with the formation of the ulcer; the count rising by $\frac{3}{4}$ -million again three days subsequently. No disturbance in the white cell picture was noted.]

Dr. EMBLETON said that, with regard to amidopyrine compounds and their toxic effects on certain individuals, it was possible that toxic effects other than those on the blood-forming tissues might occur. He had seen a female patient (aged 39) who was admitted to a nursing-home, with transitory jaundice, diarrhoea, leucopenia (4,200), anæmia (1,910,000), and suppression of urine, and who died ten days later. She had been under observation for some months, having anæmia, loss of weight, and debility, and had had several attacks of confusion and double vision. It was found that she had taken 142 tablets of allonal in six months, though there were periods of over a week at a time during which no drug could have been obtained. It was possible that she had been suffering from an intermittent amidopyrine poisoning and that the sudden onset of the terminal symptoms was provoked by a renewed exhibition of this drug.

POSTSCRIPT.—Since the meeting a rise in the blood-count in the first case has been noted, the red blood-cells reaching, on March 14, 5,260,000, and the white blood-cells 7,000, with 53% polymorphonuclear cells. This was followed, on the eighteenth day from the last neutropenic period, on April 5, with a count of red blood-cells 4,750,000, white blood-cells 3,000, polymorphonuclears 0.66%. This neutropenic period was not accompanied by any ulceration of the mouth. [D.E.]

Scleroderma.—HUGH GORDON, M.C., M.R.C.P.

The patient is a healthy man aged 65. About three months ago he noticed that the skin of his throat seemed to be getting thickened; he is quite certain that he had no sore throat. This thickening spread rapidly down his chest and back.

When first seen one month ago, the skin of the torso, front and back, was of a board-like rigidity. The induration appeared to affect the deeper layers of the dermis. There was a slight suggestion of pigmentation and atrophy on the shoulders.

Wassermann reaction negative. Blood calcium normal.

During his stay in hospital for a month, the patient was treated by short-wave therapy. The condition has now become worse; it has spread down to the legs. The chest is typically sclerodermatous; the shoulders show a bluish tinge with telangiectasia and commencing atrophy of the epidermis.

Microscopical examination shows little except sclerodermic change deep in the corium. The connective tissue is condensed and the fibrous tissue is broken up. There is a slight inflammatory reaction. No mucin was found.

Dr. HALDIN-DAVIS said that he wondered what Dr. Gordon thought about the prognosis in this case. His own view was the condition was serious, but by no means hopeless. Some years ago he had had a case of this kind under his care at the Royal Free Hospital,

and to his surprise the patient got well. After some weeks' treatment in hospital, the spread of the scleroderma ceased, leaving only plaques of scarring on the arms, chest, and back, and there was never at any time any embarrassment of respiration. The patient was treated with various forms of electricity, and also with colonic irrigation. Therefore in the present case the prognosis might not be so bad as was commonly supposed.

Scleredema Adultorum (Buschke).—HUGH GORDON, M.C., M.R.C.P.

This patient, aged 30, was shown to the British Association of Dermatologists in July 1936. Her history, briefly, is that in February 1936 she had a severe sore throat and a swollen gland under the chin. About two weeks later she noticed a tight feeling about the skin of the neck which spread rapidly down the chest and arms.

When first seen, on March 21, 1936, her face had a slightly mask-like appearance. The skin was indurated from the neck downwards, over the chest and abdomen. Induration was hardest and tightest at the neck and faded in intensity as it spread downwards over the body. On the abdomen there was a faint erythema; there was no change in pigmentation. For two months she was in hospital, where she was treated by protein shock, and she improved very considerably during that time; this improvement has been maintained. To-day there is still slight induration round the neck and breasts, but otherwise the body is nearly normal. There have, however, been two sudden relapses round the jaw. The first occurred in September, following toothache. The skin over both jaws became hard and infiltrated within three days. Considerable improvement followed extraction of teeth and treatment by radiant heat. A slight relapse occurred a few weeks ago and some more teeth were taken out; since then improvement has again taken place. There is still, however, definite hardening over both cheeks.

Comment.—I am showing this case again as a contrast to the patient with acute generalized scleroderma. When she was first seen the hardness of her skin was approximately the same as that patient's. Curiously enough, the history in that case was identical with that in this, namely a thickening outside the throat, spreading rapidly over the chest. There was, however, no history of any sore throat or infective process.

Clinically, the present case differs, in that the skin has never been so wooden nor has the epidermis ever been affected. The feeling one obtained by pressure was that there was an œdema of the deeper layers of the corium. The pathological report confirmed this. It is hoped that the patient will make a complete recovery—as appears to be the rule in cases of scleredema (Buschke). Relapses have been described, as in this case.

Discussion.—Dr. F. PARKES WEBER said that such cases were known in England a long time ago, and were called the œdematous type, or the hypertrophic type, of generalized symmetrical scleroderma. In one such case the house-physician, when the patient was admitted, thought at first that he was suffering from renal œdema. In regard to generalized symmetrical scleroderma the "puffy" or "hypertrophic" cases were thought to have the best chance of recovery.

Dr. GORDON said that the patient was being treated by pituitary extract, and he now suggested making trial of pancreatin.

Carcinoma Erysipelatodes.—HUGH GORDON, M.C., M.R.C.P.

The patient, a woman aged 50, had a radical excision of the right breast, for carcinoma, performed by Mr. Jocelyn Swan at the Cancer Hospital five years ago. Ten months ago, some recurrent nodules in the scar were treated with deep X-rays, which cured them. The patient says that some time after the X-ray treatment she noticed a flush appearing over the right breast and irritating slightly.

When she was first seen three months ago, there was a patch of circular erythema 5 in. in diameter over the right breast. The edge of this erythema was quite apparent

and slightly raised on palpation. There were similar areas on the right side of the neck and in the right axilla. The edge of these areas was not raised. The three areas were not contiguous.

A section taken from the raised edge on the breast showed dilated dermal lymphatics, packed with spheroidal-celled carcinoma cells. The patient has been treated in the Cancer Hospital with Chaoul X-rays, which accounts for the scarred appearance now seen.

There is no doubt that this is a case of the so-called carcinoma erysipelatodes, though of a very early nature, since as yet there are no signs of definite papules or vesicles, which are usually found in this condition. The three areas appear to have arisen independently and not through direct spread.

Discussion.—Dr. PARKES WEBER, referring to the case he showed to the Section some time ago, which he termed "carcinoma telangiectaticum",¹ said that his patient had more of the red telangiectatic condition than the present patient. His case was treated at University College Hospital with a light application of X-rays, with the result that the redness was partly got rid of. But the patient afterwards developed lung symptoms. At the necropsy the two layers of pleura were adherent and were thickly carcinomatous.

THE PRESIDENT said that the degree of so-called telangiectasia in these cases depended on whether the carcinoma cells invaded chiefly the blood-vessels or the lymphatics.

Atrophic Areas on Insteps and Soles with ? Telangiectases: Case for Diagnosis.—J. E. M. WIGLEY, M.B.

An apparently healthy married woman, aged 30, had suffered from chilblains for many years, and always "had a poor circulation." The chilblains had affected her fingers, but not her feet. General physical examination revealed no obvious abnormality, except bluish, cold, hands and feet. A radiogram of her chest appeared normal.

The present lesions had been present about a year, and had given her no pain or discomfort. She had noticed no redness or swelling at any time.

Symmetrically placed on both insteps and the middle of the soles of both feet are irregularly shaped areas of atrophy. Over these areas, and spreading beyond them in diminishing density, are numbers of red points. The colour can be pressed out in the majority of these, but not in some of the more central ones. They appear to be dilated vessels, or telangiectases.

I have not seen lesions like these in this situation before, and am anxious to have suggestions for diagnosis and, consequently, for treatment.

Dr. F. PARKES WEBER suggested that the circumscribed patches of skin-atrophy and the punctiform telangiectases represented a very atypical, atrophic, form of the Pick-Herxheimer syndrome.

POSTSCRIPT (25.5.37).—A biopsy was subsequently made from the foot, and Dr. Muende reports that it shows idiopathic atrophy of the skin.

Three Cases Exhibiting the Ehlers-Danlos Syndrome.—A. MURRAY STUART, F.R.C.S.Ed.

Mrs. W., aged 51 (mother), Miss W., aged 22 (daughter), and Master W., aged 11 (son). The syndrome consists of:—

(1) Friability of the skin, best seen over the patellæ where papyraceous scars have formed after slight injuries.

(2) Hyperextensibility of the joints, particularly the fingers and thumbs.

(3) Hyperelasticity of the skin. This feature is not very marked in these cases. It is best seen in the case of the boy over the clavicles.

¹ For the completed account, with coloured illustration, see F. Parkes Weber: "Carcinoma telangiectaticum", *Internat. Clin.*, 1936, 3, 146.

(4) Cyst formation: Seen in the daughter's case where cysts have formed over both heels. Attempts have been made to remove these on two occasions but they have recurred.



Master W. Papyraceous scars on knees.



Miss W. Cysts on heels.

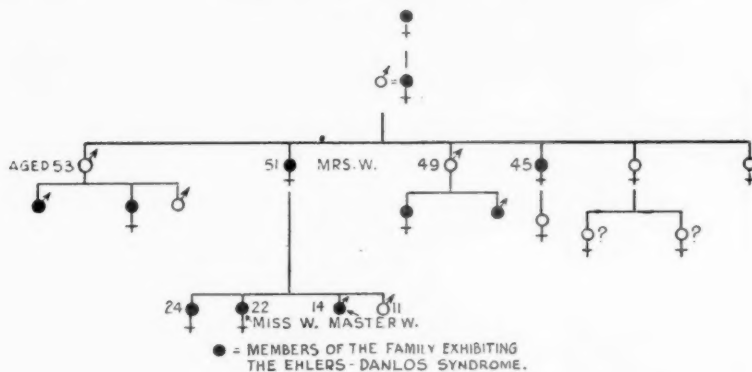
Mrs. W., an intelligent woman, gives an interesting family history. Many members of the family (as shown in the family tree) have exhibited signs over the knees and, in many cases, ? cyst formation. Her eldest daughter had "lumps"

removed from her elbows; these have not recurred. Her mother and grandmother and one sister had similar "lumps" and scars over their knees.

There has been no consanguinity in the marriages.



Miss W. Papyraceous scars on knees.



I am indebted to Dr. Neubert of St. Mary's Hospital, Portsmouth, for the photographs.

Dr. F. PARKES WEBER said he thought this was a family analogous to one which he had shown to the Section¹. Some of the cases like the present should be called "Incomplete cases of the Ehlers-Danlos Syndrome". Hyperelasticity of the skin, for instance, was more or less absent in some of them. He supposed that in the present cases there were no minute movable subcutaneous nodules, such as had been described in several cases in England.

¹ For the completed account see F. Parkes Weber, "The Ehlers-Danlos Syndrome", *Brit. J. Dermat. and Syph.*, 1936, 48, 609-617.

Section of Orthopædics

President—B. WHITCHURCH HOWELL, F.R.C.S.

[March 2, 1937]

DISCUSSION ON THE PREVENTION AND TREATMENT
OF UNUNITED FRACTURES

Mr. A. M. A. Moore: I have gone into the records of 65 cases of non-union which have been dealt with at the three hospitals with which I am associated, during the last ten years (1927 to 1936). Forty-five of the patients had been treated at some other hospital in Great Britain, and had only presented themselves for final treatment with the non-union established. I selected only those cases in which the patients were treated as in-patients, and the fracture was of, at least, six months' duration. Fractures of the neck of the femur were excluded.

General observations.—Twenty-nine cases occurred during the first half of my ten-year period, while 36 cases were dealt with during the second five years.

A Wassermann test had been carried out in thirty-nine cases, and the reaction was positive in two—one a case of fracture of the clavicle and the other of a fracture of the fibula. In the latter tabes dorsalis subsequently developed. Neither case was united with treatment.

One patient had chronic nephritis, and one rheumatoid arthritis. One developed sclerodermia, which began four months after a compound fracture of the tibia and fibula. The union did not take place with treatment and the leg had to be amputated. The patient died a year later. Except in the case of chronic nephritis, investigations of the urine did not reveal the presence of any abnormal substance. Blood-counts were carried out in 27 cases, and complete blood investigations—including a blood calcium and phosphorus and phosphatase estimate—in 19 cases. No positive results were obtained.

Influence of X-raying fractures.—It has been suggested that the taking of an excessive number of X-ray films over a short period of time may have some bearing on a case of non-union. In one case of fractured femur in a young man, who had had 45 films taken over a period of five weeks, this might have been true. As the fracture had also clearly been over-extended by skeletal traction, I feel that the number of X-ray films could not be blamed for the non-union.

Analysis of cases.

TABLE I.—UNUNITED FRACTURES (SIMPLE 46, COMPOUND 19).

Phalanx	5	Femur	12
Scaphoid	4	Tibia and fibula	12
Radius and ulna	5	Tibia only	7
Radius only	1	Fibula only	1
Ulna only	3	Metatarsals	3
Humerus	8	Rib	1
Clavicle	3		

Total no. of cases 65

Bone infection.—Radiological evidence of bone infection could clearly be demonstrated in 19 (28%). Fourteen of these occurred during the first half of the ten-year period and five in the latter half period. Eleven of the fractures were originally compound and eight were simple fractures. Of the 19 cases, in 13 the fractures had been plated or screws had been inserted, and in one an open reduction had been performed. In three there had been simple excision of wounds. Two compound fractures—one of the femur, the other of the tibia and fibula—had not had surgical treatment, and the bone destruction was so extensive that amputations had to be performed.

TABLE II.—CASES IN WHICH THERE WAS RADIOLOGICAL EVIDENCE OF BONE INFECTION.

Bone	Total	Simple	Compound	Open reduction	Plating or screw	Excision of wound	No operation
Femur	7	2	5	—	5	1	1
Tibia	4	1	3	—	3	1	—
Tibia and fibula ...	3	1	2	—	1	1	1
Humerus	4	4	—	1	3	—	—
Radius and ulna ...	1	—	1	—	1	—	—
Totals	19	8	11	1	13	3	2

It appears that surgical intervention, such as plating a fracture, was primarily responsible for the non-union in 13 out of 19 of the cases in this group.

Over-extension.—I have been able to obtain definite radiological evidence that prolonged over-extension of the fracture was employed in the primary treatment of 20 cases. Many others appear to have been over-extended, but I was not able to get the original X-ray films.

TABLE III.—CASES TREATED BY SKELETAL TRACTION.

Bone	Total	Cases of Over-extension
Femur	10	8
Tibia and fibula ...	6	3
Tibia	1	—
Radius and ulna ...	1	—
Metatarsals	1	1
Humerus	1	—
	20	12

My impression has been that, while skeletal traction is an extremely valuable method of applying extension, it has been used without due care in many cases of recent years. A short period of over-extension, for perhaps forty-eight hours, is probably of great value in securing accurate reduction of a deformity, but the amount of weight can, and should be, very considerably reduced in as short a time as possible.

Note on special fractures.—I came to the conclusion that the fractured phalanges had not been satisfactorily immobilized, and that this was probably the cause for their non-union. As regards the four ununited fractures of the scaphoid, in one case a splint had been used for some months, and in the others the wrist had been fixed in plaster which did not appear, on careful questioning, to be satisfactory for the purpose. My impression is that the most satisfactory plaster for the treatment of a fractured scaphoid is one in which the wrist is in a position of dorsiflexion and abduction, and which immobilizes the first metacarpal bone completely.

As regards the metatarsal bones, two of the fractures were missed. One had been treated by extension and I was surprised to find how relatively easy it is to over-extend the fragments in a case of multiple fractures of these bones.

Summary.—In the ten years under consideration, there were 36 cases in the latter half as compared with 29 in the earlier half. In spite of improvement in the methods of treatment, ununited fractures were occurring with greater frequency.

y be
f the
ures
n 13
ction
Two
d not
tions

on

arily

that
nt of
o get

uable
es of
rs, is
ount
sible.
anges
e for
case
fixed
the
of a
duc-

been
tend

the
n the
7.



FIG. 3.—Taken at the end of ten weeks—two weeks after skeletal was removed. End result: non-union.

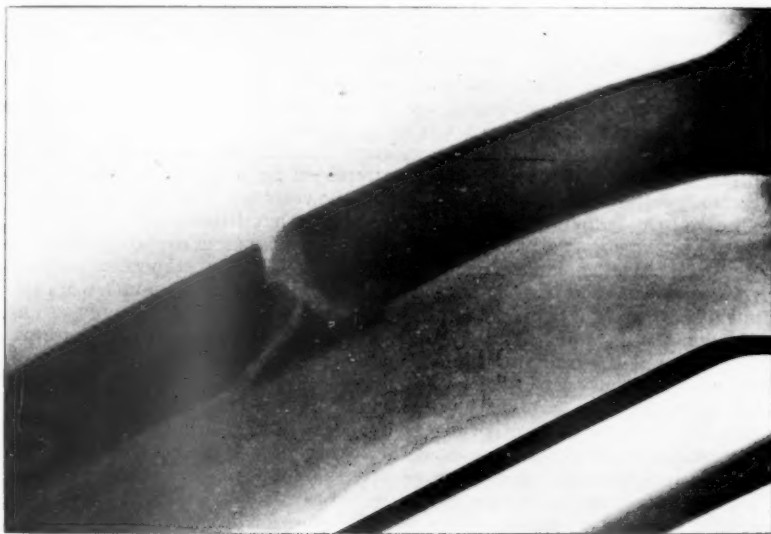


FIG. 2.—After treatment by skeletal traction for eight weeks. Result: non-union.

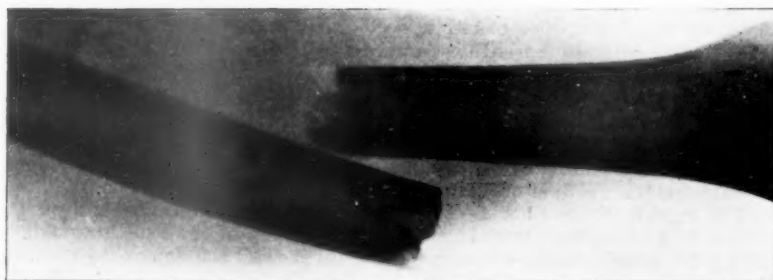


FIG. 1.—Fracture of the shaft of the femur.

No general factors could be established for the causation of non-union. Excessive X-raying did not influence it.

Where there was X-ray evidence of bone infection, 14 cases out of 19 occurred in the first five-year period, and only five in the latter half period. Of the 19 cases 14 had had surgical interference.

Twenty had been treated by prolonged skeletal traction during their early stages, and radiological evidence suggests that over-extension was the cause for the non-union in many of these.

In conclusion, I should like to thank Mr. Robt. Milne and those surgical colleagues at the London Hospital, Poplar Hospital for Accidents, and King George Hospital, Ilford, who have permitted me to make use of their cases.

Mr. H. A. T. Fairbank : Delayed union of fractures is just as frequently seen as it was twenty years ago, though resort to operation is less often considered necessary than it was. The causes of delayed and non-union are local, not general. Imperfect immobilization is undoubtedly the chief cause, but is not, as some would have us believe, the only cause. Want of apposition of fragments and deficient blood supply of one of them *are* of importance in certain cases. I am old enough to have watched the old method of prolonged use of none-too-efficient splintage, with no regard for other considerations, give way to "mobilization and massage" which, used indiscriminately—as it was then and even is to-day by some—gave just as bad results. Fortunately this has now been replaced by a method which regards immobilization, preferably by plaster splints, as the essential, but favours the early functional use of the limb, provided this is possible without disturbing the fragments. Far too many cases are still seen, however, of delayed union resulting from the too-early use of massage, and movement of adjacent joints. Another common fault, perhaps less common than it was, but still providing a certain number of cases of non-union, is to treat a simple fracture by internal fixation and not only use an insufficient number of screws, but in addition fail to provide adequate external splintage. Every plated fracture should be splinted externally with the same care, and often for the same length of time as a similar fracture—i.e. one with perfect apposition of fragments—that has been treated conservatively. I am not at all certain that the pendulum has not swung over too far and that it would not be better if open operation, which should give something very near 100 per cent. perfection in its results, were resorted to more frequently than it is to-day. At any rate I rather feel that this is true of my own practice.

Personally I regard malposition as a definite cause of delayed union and even of non-union. I have been much struck by the almost complete absence of callus formation when operating upon some cases of transverse fracture, with overlap, of the femur and forearm bones, although three or four months had elapsed since the fracture occurred. In such cases one has seen nothing more than a little rounding off of the sharp edges, yet when placed in good position and fixed, the fractures in these cases united without the slightest difficulty. Interposition of muscle, &c., between the fragments as a cause of non-union I regard as so rare as to be negligible. Once I found the musculospiral nerve between the fragments of a fractured humerus.

In recent years a new cause of non-union has appeared, namely skeletal traction. Having published a short paper [1] calling attention to this risk, I was delighted to hear the emphasis laid on this by Mr. Moore. The method is undoubtedly providing an appreciable number of non-unions even when it has been used under the best conditions as regards X-ray control. Invaluable as the method undoubtedly is in certain cases—e.g. compound fractures of the lower third of the leg—it would, I think, be a great mistake to allow students to regard skeletal traction as the method of choice in cases requiring extension.

As to treatment, the decision as to whether a case should be regarded as one of delayed union only, or of non-union requiring operation, should depend more on the X-ray appearances than on the time factor. The amount of callus and the absence or presence of sclerosis of the ends of the fragments are usually regarded as the points of greatest importance, but I feel that the position of the fragments is often the deciding factor. The tendency nowadays to favour functional use of the broken limb, even to the extent of weight-bearing, if this can be done without risking the immobilization, undoubtedly saves from operation many cases that would, a few years ago, have been treated by grafting. This holds good for cases with fairly good apposition of fragments and good alignment. Angular displacement, on the other hand, is particularly unfavourable. In the tibia, for instance, with this deformity weight-bearing is impossible without a bending strain occurring at the fracture, in spite of perfect plaster work. Again, when displacement of the fragments in a transverse fracture is complete, it often saves much time, besides giving a more perfect result, to operate while the case would still be regarded by many as only a delayed union. In such a case, operated upon relatively early, bone-grafting is unnecessary, reduction and plating being sufficient to produce rapid consolidation. I have in mind cases which might have been treated by operation at first, but which for various reasons were treated conservatively. In most cases of real non-union bone-grafting is an essential part of the operation. An inlay graft is usually considered the best type but the intra-medullary insertion of one end is often convenient and beneficial. I have used an intra-medullary graft for the clavicle with complete satisfaction in one case, and several times for the humerus and femur. In femoral cases I am accustomed, in addition to the graft, to apply a plate and at least eight screws, so as to avoid the disaster of breaking the graft while applying the splint at the end of the operation. I have had no reason to regret this course. In the case of the upper half of the ulna, the surgeon should not attempt to correct the deformity completely, and should not try to get the fragments into line. As is well known, the radius falls inwards across the upper fragment of the ulna. This displacement cannot be corrected completely without great force, and the subsequent strain on the graft, if the ulnar fragments are forced into line, will certainly result in the graft giving way. The graft should be inserted obliquely into the upper fragment, with only that amount of correction which can be achieved without strain. A living autogenous graft has—in my opinion—great advantages over all other types.

I dislike encircling bone with wire or a metal band. No surgeon can avoid absorption occurring beneath such a band or wire in some cases; if this occurs the bone is weakened to a dangerous degree.

Reference.—1 "Livre Jubilaire Albin Lambotte," Vromant et Cie., Brussels, 1936, p. 227.

Mr. G. R. Girdlestone: I wish to lay great emphasis on the importance of damage to the circulation of the bone as a cause of delayed and non-union. Union depends upon active circulation in both the fractured ends. In these cases one often sees—as, indeed, Mr. Moore's radiograms have demonstrated—the formation of a periosteal bridge of bone from the periosteum of the shaft an inch or so above the fracture to a similar position below, with a complete lack of callus matrix between the ends themselves.

Sometimes the damage to the nutrient arteries is so extensive as to lead to prolonged anæmia or ischemia of the ends. In such cases to operate prematurely is harmful and appears to postpone the return of circulation which, however, will follow a period of active use. It may be necessary to have a patient with a non-union of the femur get up with his limb in a walking appliance for some months before the circulation is re-established. Union may then occur, but if it does not, grafting can then be carried out under favourable conditions.

I feel strongly the value of the recognition of this point, for bone-grafts will often fail if the central part of their course is in an avascular bone bed. Bone-grafts have acquired a reputation for carrying circulation beyond their very considerable deserts. My colleagues and myself make a great point in the technique of grafting such cases, in avoiding the complete stripping-up of the bone-ends as we feel that the circulation in the bone-ends could be further damaged by the stripping away of the soft tissues. In many cases good joinery will succeed, but others, of the nature described, demand more biological care. In these more difficult cases my results had been better since I avoided freeing of the ends and left the distant—from the operator's point of view—side of the bone-ends undisturbed in their vascular soft tissue bed.

In advocating the now well-known method of drilling through sclerosed and relatively avascular bone, I would point out that just as passive movements may be necessary to prepare the way for active use in a joint, so, in a bone, drilling may provide channels by which active circulation may be restored. My second point is an advocacy of using not merely the Albee type of bone graft, but a combination of inlay, osteoperiosteal, and multiple small chip grafts as massively as conditions will allow.

The following table shows the results in a series of 18 cases of grafting for definitely established non-union.

END-RESULTS OF OPERATIONS FOR NON-UNION OF BONE.

Bone	No. of cases	Bony union	Non-union
Femur, shaft	3	3	—
Tibia fibula	8	7	1
Humerus, shaft	3	3	—
Ulna	2	2	—
Scaphoid	2	2	—
Totals	18	17	1

Mr. K. H. Pridie: It is a common fault to confuse delayed union and non-union, and most of the cases shown by previous speakers are simply cases of delayed union. A fracture may be said to be ununited when it will not unite without operative intervention, no matter how long it is left.

Certain types of fracture, however, will never unite without operative treatment. These are fractures of the patella, fractures of the olecranon, and intracapsular fractures of the neck of the femur, but they hardly enter into the discussion.

Certain fractures, we know, are slow in uniting. The healing time varies inversely with the cross-section of the bone at the site of fracture, and thus a transverse fracture of the femur takes longer to consolidate than a long spiral fracture where the surfaces broken are large.

It is also common to confuse the terms "union" and "consolidation". In a case of fracture of the femur a mass of callus is thrown out after five to six weeks. If traction is discontinued now, the bones will angulate at the site of fracture, but no fresh overlap will occur, as the bones are united together with a soft semi-organized callus. It is only later, when consolidation has taken place, that we can dispense with splints and allow the patient to walk without fear of angulation.

When a Fracture Clinic was opened at Bristol, there were ten cases of ununited fractures which needed treatment. Since then, 4,000 fractures have been treated and only one has failed to unite. This was an intracapsular fracture of the neck of the femur where the Smith-Petersen pin slipped out, as the head fragment was too small.

An investigation of the ununited fractures which have been sent to the Clinic for treatment, shows that the most common cause of non-union is over-traction. In three cases which had been treated with 30 lb. traction for six weeks the bones had been pulled over length and non-union had resulted.

Cases of non-union can be treated simply by multiple drilling of the bone-ends, using a high-speed electric drill. The drill-holes re-vascularize the bone-ends, and union takes place rapidly, provided that splinting is adequate. The modern tendency is to diagnose those cases in which delayed union is likely to occur and perform a bone-drilling operation to ensure speedy union.

Mr. Eric Lloyd had used Beck's drilling six times, three of which were in cases of fractures of the tibia. All were cases of non-union of some standing and in each the fibula was divided and the tibia drilled. Two were successful and one had been a failure to date.

Case I.—Man aged 20. Non-union of 2½ years' duration. Walked in plaster after Beck's drilling and seven months later the bone was clinically and radiologically united. Plaster was continued for two months and the patient has worn no support for the last three months and is now able to run painlessly.

Case II.—Man aged 27. Non-union of one year and eight months' duration. The patient, unfortunately, was allowed to walk in a plaster which did not include foot or ankle, and as the fracture had failed to unite in eleven months it was again drilled and he is now walking in plaster, though the result is still awaited.

Case III.—Man aged 24. Non-union of one year and five months' duration. Walked in plaster day after Beck's drilling and four months later was clinically and radiologically united. All support was discarded and when seen three months later he was walking perfectly well.

POSTSCRIPT (20.3.37).—This patient has now relapsed and consolidation is incomplete. He is being provided with a double short walking-iron but a bone-graft may still be necessary later.

All three patients had apparently been treated by skeletal traction at the time of the fracture and one of them (the patient in Case III) said that he had had 35 lb. traction for five weeks.

Mr. St. J. D. Buxton said that he had investigated the 24 cases of non-union, and delayed union, of the tibia, that had been under his care during the period 1928–1935.

In two cases of non-union in infants bone-grafting had been carried out; in neither had the fracture united and in one the limb had since been amputated. Two transverse tibial fractures had been treated by provision of a moulded leather splint and side-irons, months after the fracture, and in both the bone had joined. Twenty cases had been bone-grafted, by a slide-graft from the same tibia. Union occurred in every case. No internal fixation was employed, but the fibula was invariably divided and the tibia approximated after removal of sclerosed bone. A bridge of bone, half an inch wide at the lower end of the proximal fragment, was left below the area from which the graft was cut. This helped the firm fixation of the graft, which was an essential part of the operation. A number of these patients were now playing football, cycling, and doing hard labouring work. A few complained of stiffness of the ankle, and periodic swelling.

The President agreed that there had been non-union in cases in which the ends of the fracture had been distracted by skeletal traction either too severe or too prolonged, without due regard having been paid to the necessity of impacting them

when the correct length and position had been obtained. Periosteum, muscle, and other structures were sometimes interposed between the ends of the bone, and for that reason open operation, and not drilling of the bones subcutaneously, was essential. The best results in the treatment of non-union were obtained by open operation, the periosteum being stripped extensively up and down the shaft, the ends of the bone freshened, and a long, wide, and massive, autogenous bone-graft inserted within the "cigarette tube" of periosteum thus prepared.

United Services Section

President—Surgeon Rear-Admiral J. FALCONER HALL, C.M.G.

[March 8, 1937]

Respiration in High Flying

By Group Captain G. STRUAN MARSHALL, O.B.E., M.R.C.S.,
L.R.C.P., R.A.F.*Consultant in Applied Physiology, R.A.F.*

ABSTRACT.—Atmospheric pressure falls, as height increases, to about one-ninth of its sea-level value at 50,000 feet. The intake of oxygen into the blood depends on the partial pressure of oxygen in the inspired air, which is about one-fifth of the atmospheric pressure. But since the gaseous content of the lungs is saturated with water vapour at body temperature, 47 mm. Hg. of the atmospheric pressure in the lungs is due to water vapour and is therefore not available for oxygen or other gases, while the alveolar air contains also an almost constant pressure of 40 mm. CO₂.

Mental and physical output demand an adequate partial pressure of O₂; they begin to be limited as soon as this falls, and at heights above 18,000 feet are seriously reduced. Consequently in order to fly higher than about 15,000 feet it is necessary to increase the partial pressure of oxygen in the inspired air. Up to about 44,000 feet this can be done by merely raising the percentage of oxygen, usually by allowing a regulated stream of oxygen to enter a small naso-buccal mask, but preferably by a closed system in which the negative pressure of inspiration opens a valve and allows oxygen to enter a bag from which it is inspired.

Beyond 44,000 feet as a limit (and a lesser height for safety) it is necessary to create a local atmospheric pressure around the pilot higher than that of the surrounding air, by enclosing him in an airtight suit or cabin in which a relatively increased pressure with a maximum value of about 2½ lb. per square inch is maintained, while he breathes pure oxygen. This device was used in the recent British world record high flight, when a height of 50,000 feet was attained. The pressure-suit used by the pilot on this occasion and the decompression chamber recently built at Farnborough are described in detail.

RÉSUMÉ.—La pression atmosphérique diminue avec l'altitude, et atteint à 15,200 mètres seulement environ 1/9 de sa valeur au niveau de la mer. La quantité d'oxygène entrant dans le sang dépend de la pression de l'oxygène dans l'air inspiré, qui comporte environ 1/5 de la pression atmosphérique. Mais comme le contenu gazeux des poumons est saturé de vapeur d'eau à la température du corps, une pression égale à 47 mm. Hg est due à la vapeur d'eau, et, par conséquent, n'est pas disponible pour l'oxygène ou d'autres gaz, et, de plus, l'air alvéolaire contient une tension à peu près constante de 40 mm. de CO₂.

L'activité physique et mentale demande une pression suffisante d'O₂; elle commence à être limitée dès que celle-ci diminue, et à une altitude de plus que 5,500 mètres elle est gravement réduite. Par conséquent, pour monter plus haut que 4,600 mètres environ, il est nécessaire d'augmenter la pression d'oxygène dans l'air inspiré. Jusqu'à une altitude d'environ 13,400 mètres il suffit d'augmenter la proportion d'oxygène, généralement en faisant passer un courant réglé d'oxygène dans un petit masque naso-buccal, mais il est préférable d'employer un appareil fermé, dans lequel la pression négative due à l'inspiration ouvre une soupape qui permet à l'oxygène d'entrer dans un sac d'où il est inspiré.

Au delà de 13,400 mètres au plus (et à une altitude moins haute pour plus de sûreté) il est nécessaire de créer une pression atmosphérique locale plus haute que celle de l'entourage, l'aviateur étant enfermé dans un scaphandre ou dans une cabine où une pression relativement

haute, de 130 mm. Hg au maximum, est maintenue, pendant qu'il respire de l'oxygène pur. Cette méthode a été employée pour obtenir le record d'altitude récemment, quand une altitude de 15,200 mètres fut atteinte. Le scaphandre porté par l'aviateur à cette occasion et la chambre à décompression récemment construite à Farnborough sont décrits en détail.

ZUSAMMENFASSUNG.—Der Luftdruck nimmt mit zunehmender Höhe ab und beträgt um einer Höhe von 15,200 Meter etwa 1/9 seiner Dichte in Meereshöhe. Die Sauerstoffaufnahme des Blutes hängt von dem Sauerstoffpartialdruck in der Einatemungsluft ab; dieser beträgt etwa 1/5 des Luftdruckes. Da jedoch die in den Lungen befindliche Luft bei Körpertemperatur mit Wasserdampf gesättigt ist, ist 47 mm. Hg des in der Lunge herrschenden Gasdruckes dem Wasserdampf zuzuschreiben und kommt dementsprechend weder für Sauerstoff noch für die anderen Gase in Betracht, während die Alveolarluft überdies einen fast konstanten Gehalt von CO_2 von 40 mm. Druck aufweist.

Geistige und körperliche Arbeit erfordern einen hinreichenden Sauerstoffpartialdruck: sobald dieser fällt, tritt eine Beeinträchtigung der Arbeit ein und in Höhen über 5,500 Meter wird die Arbeitsmöglichkeit beträchtlich eingeschränkt. Um das Fliegen in Höhen über 4,600 Meter zu ermöglichen ist daher eine Erhöhung des Sauerstoffpartialdruckes in der Inspirationsluft notwendig. Bis zu einer Höhe von 13,400 Meter kann dies dadurch erreicht werden, dass man lediglich den Prozentgehalt an Sauerstoff erhöht; die übliche Methode hierfür besteht darin, dass man einen regulierten Sauerstoffstrom in eine kleine, Nase und Mund bedeckende Maske einströmen lässt; besser ist es aber ein geschlossenes System zu verwenden, bei dem der bei der Einatmung bestehende negative Druck ein Ventil öffnet und dem Sauerstoff den Eintritt in einen Sack freigibt, aus dem er eingeatmet wird.

In Höhen über 13,400 Meter als untere Grenze (und zur Erhöhung der Sicherheit auch in geringeren Höhen) ist es notwendig, in der Umgebung des Flugzeugführers einen Atmosphärendruck zu erzeugen, der höher ist als der der umgebenden Luft; dies geschieht dadurch, dass man ihn in eine luftdichte Ausrüstung oder in eine luftdichte Kabine einschliesst, in welcher dauernd ein relativ erhöhter Druck herrscht (Maximaldruck etwa 130 Millimeter Hg), während der Flugzeugführer reinen Sauerstoff einatmet. Diese Anordnung wurde bei dem kürzlich vorgenommenen Britischen Welthöhenrekordflug verwendet, bei dem eine Höhe von 15,200 Meter erreicht wurde. Die luftdichte Ausrüstung, die von dem Flugzeugführer bei dieser Gelegenheit verwandt wurde, sowie die kürzlich in Farnborough gebaute Dekompressionskammer, werden ausführlich beschrieben.

MAN is, at least relatively, an intelligent animal, which may be defined as one having the capacity consciously to adapt himself to his environment. He is physiologically equipped for living at an atmospheric pressure normally varying from about 700 to 800 mm. Hg, but, as in most other respects, his equipment enables him to function in environments varying widely from the normal, and provides for ultimate adaptation to even wider variations without the exercise of intelligence. This is illustrated by the fact that any healthy man can ascend to a height of 10,000 ft. without serious embarrassment, and even such embarrassment as then occurs gradually disappears as he becomes acclimatized to that height. The highest level at which man continues to exist for any considerable length of time is about 18,000 ft., but such men as do so become physiologically adapted in respect of pulmonary ventilation, cardiac function, blood content, &c. The work of the numerous Everest expeditions has shown that, given the right degree of acclimatization, man can for a limited time perform prodigies of endurance and effort at much greater heights than this.

Up to a height of about 36,000 ft. (11 km.) atmospheric air contains an almost constant proportion of about 21% of oxygen. Since air is a mere mixture of relatively light and heavy gases, it is at first difficult to understand why its composition should remain thus unaffected by gravity. The explanation lies in the fact that the heating of the atmosphere by radiation, conduction, and convection from the earth ceases to be effective about that height, so that from that level upwards there is none of the vertical churning of the atmosphere caused by convection currents in the region beneath it.

Since the physical conditions of the atmosphere are variable with time and geographical position, it has been necessary to formulate an International Standard Atmosphere, representing with fair accuracy average conditions over the whole world. The atmosphere is divisible into two regions: the lower, or troposphere, in which temperature varies with height, falling (according to this Standard Atmosphere) at a rate of 3.6°F. per 1,000 ft. (6°C. per km.) from 59°F. (15°C.) at sea-level to -70°F. (-56.5°C.) at 36,090 ft. (11 km.), and the upper, or stratosphere, in which temperature is assumed to be constant. Thus we may infer that there are continual convection currents in the troposphere, and that it is these which keep the lower atmosphere in constant movement and so prevent its separation into light and heavy constituent gases.

The density of the atmosphere varies with height according to a rather complex formula. The right-hand curve of fig. 1 shows graphically the relation between height

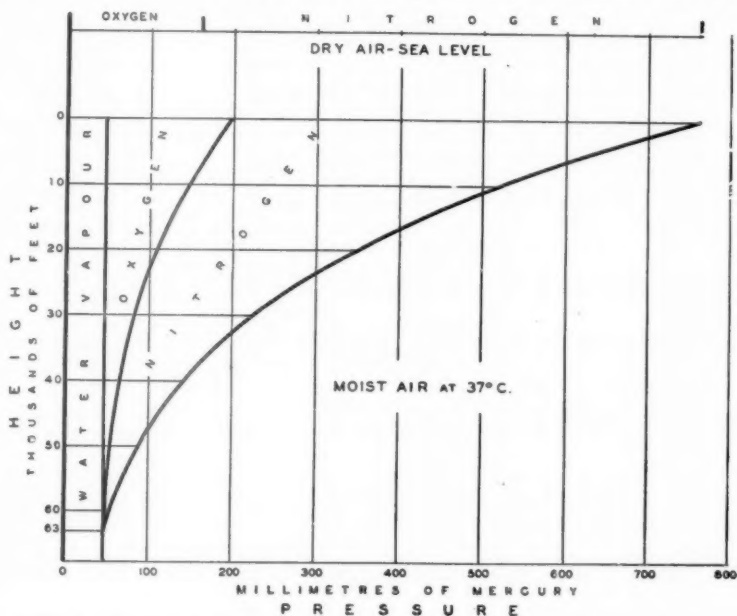


FIG. 1.—Diagram illustrating partial pressures in dry air, and in air saturated with water vapour at body temperature.

and atmospheric pressure, calculated according to the calibration law of the International Commission for Air Navigation. From this it will be seen that atmospheric pressure falls as height increases, the rate of fall being greater near the ground; it is, in fact, about eight times greater at sea-level than it is at a height of 60,000 ft. Thus at 19,000 ft. the atmospheric pressure is half, and at 34,000 ft. one quarter, of what it is at sea-level.

The atmosphere near the earth consists almost entirely of nitrogen and oxygen, with traces of carbon dioxide, hydrogen, and neon, and a relatively large amount of argon—nearly 1%. So far as is at present known, this argon has no physiological significance, but it would be idle on that account to deny it consideration. The atmosphere contains also a variable amount of water vapour, according to the

meteorological conditions, averaging about 1.2% at sea-level (though not in close proximity to the sea) and falling away to a negligible amount at or below 33,000 ft. So far as its gaseous constituents are concerned, the composition of the atmosphere remains almost unaltered up to a height of 36,000 ft., because of the temperature gradient and consequent vertical currents, but in the stratosphere (or "isothermal region", so called because in it the temperature is presumed to be constant) the composition of the air varies. The oxygen content at sea-level is about 21%; at a height of 50,000 ft. (15 km.) it has fallen to 19.6%, and at 100,000 ft. (30.5 km.) to 15.2%—here the nitrogen has risen to 84.3%, the carbon dioxide has disappeared, the trace of hydrogen present at sea-level has risen to 0.2%, and a trace of helium has appeared. At about 330,000 ft. (100 km.) the atmosphere is almost pure hydrogen.

As there is virtually the same percentage of oxygen in the atmosphere at great height as near the earth, it would at first sight appear that respiration should function just as well there. But oxygen does not pass into the blood-stream of its own accord; it needs some force to make it do so, and this force is derived from the difference in the oxygen pressure in the atmosphere and in the blood. Dalton's laws tell us that in a mixture of gases in any space the pressure exerted by any component gas is equal to the pressure which that quantity of the gas would exert if it alone occupied, and therefore filled, the space. Now all the quantities of the various components added together are equal to the volume of the space. Consequently the pressure exerted by any gas in a mixture of gases is the same fraction of the total pressure that its volume is of the total volume, that is, it is the same as the volumetric percentage. Thus, in atmospheric air at its "normal" pressure of 762 mm. Hg, containing 21% of oxygen, there is a "partial pressure," as it is called, of oxygen of 21% of 762, or 160 mm. Hg. Hence the oxygen tension in no part of the blood, under "normal" conditions, can exceed 160 mm. Actually it is everywhere far less than this, being about 80 mm. in arterial blood, 50 mm. in venous blood, and still less in the tissues.

There is yet another factor. When liquid is exposed in a confined space it begins to evaporate. Even if the remainder of the space is filled with gas, at no matter what pressure, some of the liquid will evaporate, and this process continues until the pressure of the vapour in the space is such that the rate at which the molecules of liquid enter the gas is the same as that at which the molecules of liquid already in the gas (i.e. the vapour) return to the liquid. This pressure is not, as in the case of gases, a function of the amount of liquid present (provided that all the liquid is not evaporated, i.e. that there is still some—no matter how little—free liquid left in contact with the gas) but depends solely upon the nature and the temperature of the liquid. Thus, water at a temperature of 98.4° F. (37° C.) exerts a maximum pressure of 47 mm. Hg—that is, so long as any free water remains, the pressure of the water vapour is 47 mm. Hg.

Consequently, if we assume—and if this assumption is not academically correct it is at least in fair accord with the observed facts—that on reaching the pulmonary alveoli the incoming air has a temperature of 37° C. and is fully saturated with water from the moisture constantly present throughout the respiratory tract, it is clear that no matter what the nature or pressure of the inspired air there is present in it water vapour at a pressure of 47 mm. Hg (see fig. 1). Hence at the "normal" barometric pressure of 762 mm. Hg there is a total gas pressure in the lungs of 762–47, or 715 mm. Hg. But the gaseous components divide the total gas pressure between them in proportion to their percentages. Therefore, if we wish to determine the true partial pressure of oxygen in the air when it reaches the alveoli (setting aside for the moment the fact that before reaching the alveoli it will have mixed with expired air of different composition) we must first deduct 47 mm. Hg from the atmospheric pressure and then take 21% of the difference—at sea-level this becomes 21% of 715 = 150 mm. Hg.

The amount of oxygen present in the blood is, within certain limits, a function of the amount of hæmoglobin in the blood, and the pressure of oxygen to which the blood is exposed. The upper limit is reached when the hæmoglobin is fully saturated with oxygen, of which it can take up about 1.34 c.c. per gramme. Arterial blood is not quite fully saturated, containing only about 96% of the amount representing full saturation. As the pressure of oxygen in the alveoli falls, the degree of saturation also falls, but not proportionately, the fall in saturation being relatively small until the oxygen pressure has fallen to about half of that necessary for full saturation. About this point the degree of saturation begins to fall off very rapidly as the oxygen pressure continues to fall.

Experiments in "doping" athletes with oxygen indicate that although man can carry on very well with a considerable fall in oxygen pressure from the normal, the slightest fall means some slight diminution of maximum power output. This does not usually affect the pilot flying at heights below 15,000 ft. (4.6 km.), where the atmospheric pressure is about 430 mm. Hg, because he has little physical work to do, but even at these relatively low levels there is reason to believe that mental processes are perceptibly slowed, and if so, it can only be the drop in partial pressure of oxygen that is responsible, provided that the subject is kept warm.

At a height of 15,000 ft. the oxygen pressure in the wet inspire (that is, in inspired air saturated with water vapour at a temperature of 37° C.) is about 80 mm. Hg, and at 20,000 ft. about 64 mm. Hg, the corresponding oxygen pressures in the alveolar air being about 50 and 36 mm. Hg respectively, and the respective degrees of saturation of the blood with oxygen about 82% and 63%. In practice it is found that the limit of safety lies somewhere between these two heights, and this is in accord with experiments where samples of alveolar air were taken after a short stay at different heights (or their equivalents in reduced atmospheric pressure artificially produced in a decompression chamber). In these experiments it was found that so long as the oxygen pressure in the alveolar air remained above 50 mm. Hg the subject was comfortable; with alveolar oxygen pressures between 50 and 40 mm. Hg there was some degree of distress, between 40 and 30 mm. Hg severe distress, and unconsciousness usually at or rather above 30 mm. Hg. For these reasons pilots of the Royal Air Force are not permitted to fly, breathing only atmospheric air, above 16,000 ft.

Above this height it is necessary to provide some means of increasing the oxygen pressure in the alveolar air, which means, in effect, in the inspired air. The simplest way to do this is to increase the percentage of oxygen in the inspired air, and this is commonly done by allowing a regulated stream of oxygen to enter a suitable mask secured over nose and mouth, and there to mingle with the inspired atmospheric air, which enters the mask through two apertures of suitable size. The oxygen for this purpose is carried either liquid in Dewar flasks or compressed in light cylinders of special high-tensile steel, the latter method being preferred on account of the difficulty of supplying liquid oxygen in the field. The oxygen from the cylinder, in which it is compressed to 120 atmospheres or about 1,800 lb. per square inch, passes to a pressure-gauge of the usual pattern, incorporating a filter, then through a heater, whose primary object is not the comfort of the pilot but the avoidance of the blockage of the valves by formation of ice from the minute trace of water that is almost inevitably present in compressed oxygen, to a reducing valve, from which it emerges at a predetermined pressure of about 20 lb. per square inch. It then passes through a flowmeter, calibrated in thousands of feet according to the rate of flow calculated to be necessary at the respective height levels, and then by way of a rapid-release bayonet joint to the mask.

This method is fairly satisfactory for moderate heights, but it has certain disadvantages. Since inspiration occupies only about one-third of the respiratory cycle, and the flow of oxygen is constant, it is clear that for two-thirds of the time of use the

oxygen is merely pouring out to waste, so that provision must be made for carrying three times as much oxygen as is actually used. But there is a more serious disadvantage in this open method of administration. The rate of oxygen consumption required for only moderate physical work greatly exceeds the consumption during the relative inaction of piloting an aircraft, and this increased requirement is manifested by increased respiration. Thus a larger volume of air passes through the nostrils of the mask in unit time, while the volume of additional oxygen delivered by the supply apparatus in unit time remains unaltered. Consequently the mixture entering the lungs becomes poorer in oxygen when physical output is increased, i.e. the partial pressure of oxygen in the inspired air decreases and a vicious circle is established, for the response to lack of oxygen is panting, and this increases still further the relative lack of oxygen in the inspired air.

Hence this open-mask method of administration of oxygen is one which requires adjustment according not only to the height, but also to the rate of doing work. This is a serious drawback in the Service, where the rate of doing physical work cannot be accurately forecast from one minute to the next, so that when there is any immediate prospect of heavy exertion, the subject must increase the rate of oxygen flow beyond that calculated as necessary for the height at which he is flying.

A better method is to make use of the lung-controlled principle, in which oxygen passes by way of a very fine valve into a small rubber bag about the size of a small hot-water bottle, from which it is inspired. The act of inspiration deflates the bag and so causes two light wire frames inside it to approximate, thus opening the valve and allowing the bag to refill with oxygen, when the separation of the wire frames closes the valve and stops the oxygen flow. The subject breathes through inspiratory and expiratory valves, so that his expirate does not mix, outside the body, with his inspire. In this connexion it is interesting to note that the inspiration of oxygen instead of air does not of itself alter the pulmonary ventilation, yet it is a remarkable fact that in using such an apparatus at an atmospheric pressure of about 140 mm. Hg, which corresponds with a height of 40,000 ft., I have more than once observed that the subject has stopped breathing. This cannot be analogous to the apnoea following on forced breathing, whereby the carbon dioxide is excessively washed out of the system, since there is no excessive pulmonary ventilation and the carbon dioxide content of ordinary air is too small to have any physiological significance. So far as I can trace, this phenomenon has not been previously reported, nor can I offer any theory to account for it. It could, no doubt, be avoided by adding a small percentage of carbon dioxide to the oxygen used, but its causation would still be obscure.

Now this process of preventing the oxygen want that would otherwise inevitably occur in high flying by raising the oxygen content of the inspire is satisfactory up to the point where the oxygen percentage is 100 and the height such that the total atmospheric pressure is equal to the partial pressure of oxygen in ordinary air at about 18,000 ft. Fig. 1 (p. 11) shows that this height is about 44,000 ft., and it is interesting to note in confirmation that a young, healthy, and experienced subject fainted in the decompression chamber, when breathing only oxygen, at a pressure corresponding to a height of 44,000 ft.

What, then, is to be done to enable men to fly above this height? We cannot increase the percentage of oxygen beyond 100, and we must therefore create around the pilot an artificial atmospheric pressure which never falls below some arbitrary value well above that corresponding with our limit of 44,000 ft., or about 120 mm. Hg. This can be done by enclosing him in either an airtight cabin or an airtight suit, in which the pressure is raised above that of the surrounding atmosphere to a constant absolute value. For technical reasons of aircraft construction, the airtight cabin is the less practicable of the two, as the relatively large size of an aircraft cabin demands considerable additional strength to enable it to withstand the added internal

pressure over so large a surface, and this means too much weight. Use is therefore made of a sort of diving suit (fig. 2) made of rubberized fabric, fitted with a helmet of the same material, with a large curved double window. The suit is made in two pieces, upper and lower, joined at the waist by means of a flexible steel band (2, A) which is tightened on to a rigid hoop, clamping the two layers of fabric together. The space between the two layers of the window is kept dry, in order to prevent the formation of mist or ice where it would obstruct vision, by means of a drying-tube (2, B) at the side of the helmet, the air passing into and out of this space, by way of the

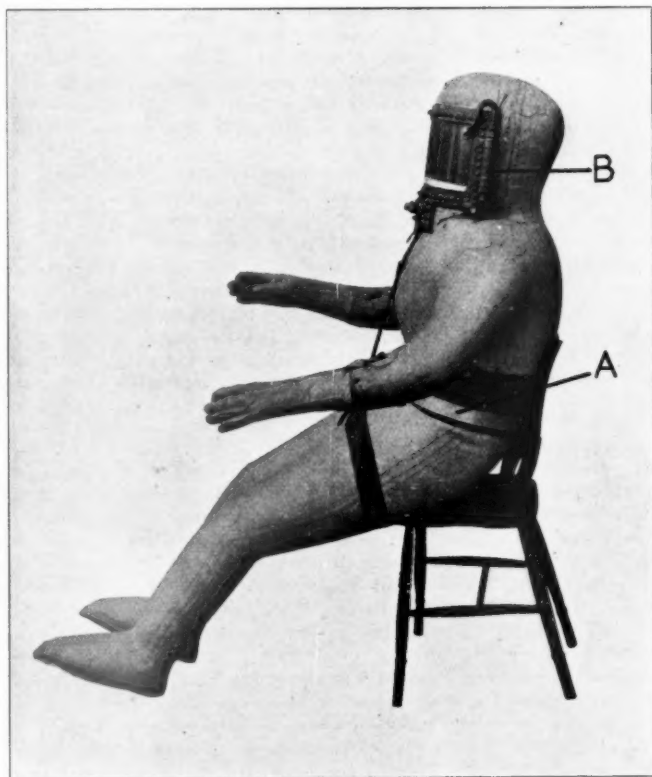


FIG. 2.—Pressure Suit for flying at very high altitude. A, steel waist-band sealing joint between two halves of suit; B, drying-tube.

(Crown copyright reserved.)

drying-tube, as the barometric pressure rises and falls. The pilot breathes nothing but oxygen, which is supplied by means of an injector which ensures circulation through a soda-lime canister. This absorbs both carbon dioxide and water, and incidentally warms the circulating oxygen in doing so. The pressure within the suit is automatically adjusted so as not to exceed a fixed value of about $2\frac{1}{2}$ lb. per square inch, or 130 mm. Hg, above that of the surrounding air. The oxygen pressure in the dry inspirate is therefore always at least 130 mm. Hg even in a vacuum, and

is thus able to support life at infinite height. At a height of 80,000 ft. (24.2 km.), which is considerably higher than any aerodyne¹ is likely to attain for some time to come, the pilot will receive oxygen at a pressure of 150 mm. Hg, and is therefore under similar physiological conditions to those when flying without oxygen at about 9,000 ft. (2.7 km.)—a height no greater than is habitually attained by many commercial aircraft. This internal pressure-difference must not be too high, or it would seriously impede the movements of the pilot's limbs; at the value prescribed the wearer is easily able to make every movement required in piloting.

It may be asked why the necessary additional oxygen pressure in the lungs cannot be provided more simply by supercharging the pilot. An internal-combustion engine can be supercharged in order to increase the mass of mixture entering the cylinder, and it might be practicable to apply this method to the lungs were it not for the fact that a small increase of intrapulmonary pressure impedes the pulmonary circulation and causes an intolerable resistance to expiration. But if the pressure is applied outside the trunk as well as inside it this objection disappears, and this is in fact what is done in the pressure suit.

When existence under reduced atmospheric pressure is prolonged, there is an increase in the number of red corpuscles with a corresponding increase in the amount of haemoglobin in the body. This is one of the adaptations which make it possible for mountain climbers to ascend gradually to, and live in tolerable comfort at, much greater heights than would be possible if they were suddenly transported there, as in an aircraft. This, however, is a relatively slow process, and has but little application to high flying. It is true that frequent and prolonged flights at as great heights as are permissible without oxygen will bring about a small increase in the red cell count, but this is only transient, and the increase in oxygen capacity of the blood thus gained is of but little practical value, as it adds only a few thousand feet to the pilot's ceiling.

DECOMPRESSION CHAMBER

In order to test the applicability of these theoretical considerations, and for other experimental purposes, use is made of a decompression chamber. There are many of these in different countries, owned by governments, universities, and private firms or individuals, and they are used for many studies other than physiological. The Air Ministry has three, of which the one now to be described is at the Royal Aircraft Establishment, South Farnborough, Hampshire, and was designed primarily for physiological purposes. This chamber (fig. 3) has proved in use to be so well designed that I cannot suggest a single particular in which alteration would make it more suitable.

The chamber consists of a cylindrical vessel, with axis vertical, measuring internally 8 ft. 2 in. high by 7 ft. 0 in. diameter (249 × 213 cm.). The top and bottom, which in such chambers are usually domed to resist pressure from without, are here made of flat steel plate $\frac{3}{4}$ in. thick (1.8 cm.), each reinforced with four channel-steel joists, and the walls are of $\frac{5}{8}$ in. (1.6 cm.) steel plate. A door of $\frac{5}{8}$ in. steel plate, reinforced with angles and measuring 6 ft. 3 in. by 2 ft. 0 in. clear (191 × 61 cm.), is set in a slightly projecting framework and hung on hinges slightly slotted to allow of the necessary play in making it airtight on closing. It beds on to a rubber joint $\frac{1}{2}$ in. thick (1.3 cm.), and is held into position by two hand screws. These screws are necessary only at the beginning of evacuation, since the differential pressure on the outside of the door, which tends to force it shut, soon becomes far greater than could be produced by the screws. Since the area of the doorway is $12\frac{1}{2}$ sq. ft. (1.2 sq. m.), an internal pressure reduced to correspond with a height of only 5,000 ft. (1.5 km.) causes an atmospheric pressure on the outside of the door of 2 tons, while at 30,000 ft. (9.1 km.) the pressure is over 10 tons. In the upper half of the door is a

¹ Aircraft heavier than air.

window 1 ft. 6 in. high by 9 in. wide (46×23 cm.) of $1\frac{1}{8}$ in. plate glass. The capacity of the chamber, including the spaces beyond floor and ceiling, is 400 cubic feet (11.3 cu. m.).

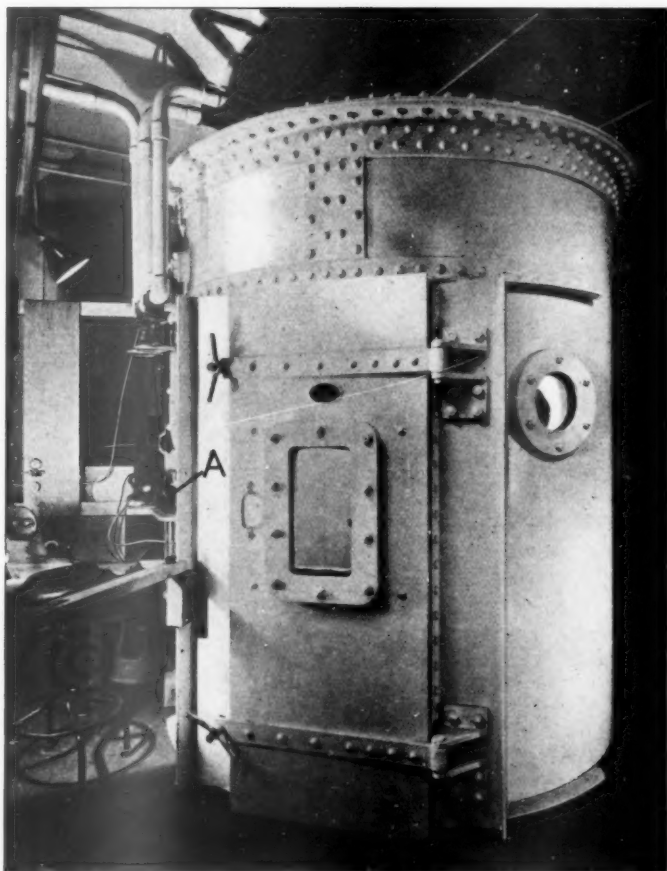


FIG. 3.—Decompression Chamber, R.A.E., Farnborough. A, device for showing rate of ascent or descent.

(Crown copyright reserved.)

Equally spaced around the circumference are four 9-in. circular windows of $\frac{7}{8}$ -in. plate glass (fig. 4, D, p. 18), placed 5 ft. above external ground level, with a fifth at 3 ft. 8 in., the purpose of the latter being close observation of experimental subjects, especially to detect incipient cyanosis. All windows are permanently closed and airtight. The ceiling and floor are of wood. The chamber is lined throughout with $\frac{1}{4}$ -in. felt, which is white on walls and ceiling in order to reflect the maximum amount of light; without this felt the echoes make conversation in the chamber almost unintelligible. The internal lighting is by four separate 100-watt daylight blue lamps

in porthole-type fittings; this is quite enough to enable the onset of cyanosis, which is invisible in the yellow light of ordinary bulbs, to be detected. All electric leads are passed through the walls by way of airtight glands. In the wall of the chamber are four short pipes (fig. 4, A) closed with screw caps when not in use, through which any necessary additional tubes or electric leads can be passed in suitable packing. Three low-tension electric terminals (fig. 4, B) are provided for experimental apparatus—common negative, and 6-volt and 12-volt positives.

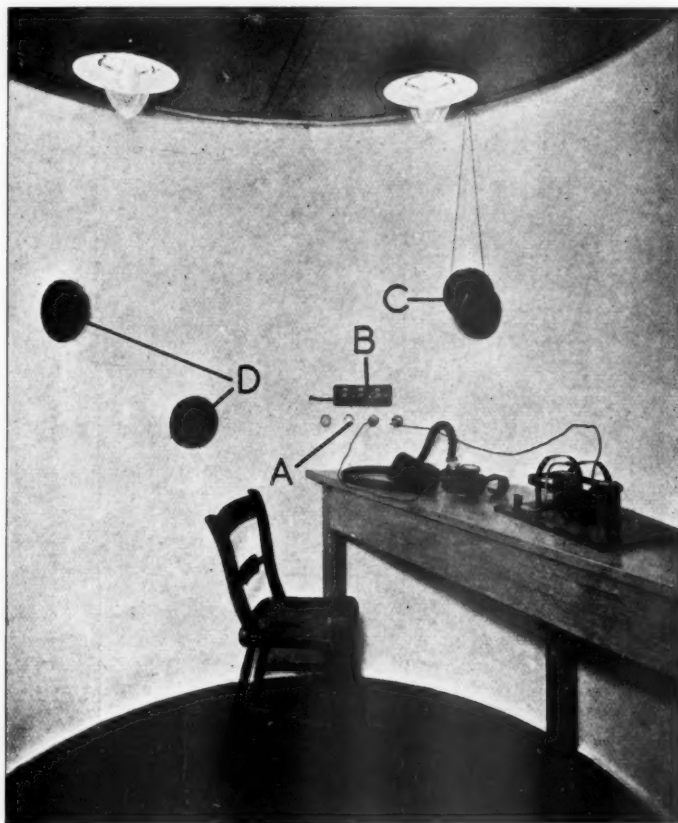


FIG. 4.—Decompression Chamber, interior. A, air-tight conduits for passing pipes, &c., through the wall; B, low-tension electric terminals; C, altimeter; D, observation windows. (Crown copyright reserved.)

The machinery required to operate this chamber consists of a water-cooled reciprocating pump driven through a heavy flywheel by a $7\frac{1}{2}$ -h.p. electric motor, having a volumetric capacity of 148 cu. ft. (4.2 cu. m.) per minute. This is capable of reducing the pressure in the chamber to $\frac{1}{4}$ lb. per sq. in. (12.7 mm. Hg), corresponding to a height of 90,000 ft., while maintaining at the same time a ventilation rate of $\frac{1}{2}$ cu. ft. (14 litres) of free air per minute, which is equal to sixty times as much

of the attenuated air in the chamber under such conditions. Ventilation at such a "height" is of no consequence for the replacement of used oxygen, because no one could survive exposure to so attenuated an atmosphere, even if he were to breathe pure oxygen. At lesser heights, however, this ventilation is of value, since it serves to reduce the humidity of air caused by the sweat and exhalations of the occupants, which would otherwise make the heat produced by the recompression of the air on returning to normal pressure almost intolerable.

The 2-in. suction pipe from the pump (fig. 5, A, p. 20) divides into two branches; one (B) goes through a valve to the outer air, and the other (C) through a valve to the chamber, where it enters above the ceiling through a Burgess silencer and two flame-traps, arranged in series and having an effective area of 16 sq. in. Another, but independent, pipe (D) connects the chamber direct with the outer air through a valve (E), with a branch connexion for flooding the chamber with oxygen in emergency. These safety measures are by no means to be despised; on at least one occasion they have averted what might have been a tragedy.

The pump runs at constant speed and the atmospheric pressure in the chamber is controlled entirely by the valves. When the pressure is to be kept constant, as is usually the case in experimental work, but with no ventilation, the suction pipe leading to the pump is therefore closed, thus relieving the pump of work, for it quickly establishes an almost perfect vacuum on each side of the pistons, and then does virtually no work at all.

Great care has been given to the comfort of the operator in order to ensure that his attention will not be distracted. One man alone is needed for the entire operation of the chamber. He sits on a specially designed seat with all gauges within his field of vision and all controls accessible without stretching. The seat is adjustable in height to bring the operator's eyes to a convenient level, and since he has a 9-in. porthole window 5 ft. above the floor he can change to a standing position at will, and so relieve the tedium of prolonged sitting. A strong light above his head is directed on to the gauges and controls, a telephone is at his hand in case he may need assistance, and a red button (F) at his side serves to stop the pump instantly in emergency. At his side is a loud-speaker (G), and there is another inside the chamber, so arranged that the one in the chamber normally acts as a microphone, the one outside broadcasting every sound made in the chamber. By pressing a button (H) the operator can exchange the respective roles of the two loud-speakers and can thus speak to the occupants.

The gauges consist of an altimeter (fig. 4, C,) in the chamber, which can be read from without as well as from within, while outside the chamber, within sight of the operator, are a device (fig. 3, A, p. 17) for showing the actual rate of ascent or descent at any moment, a pressure-gauge, a mercury manometer, and a large oxygen cylinder (fig. 5, J) with pressure-gauge (K) and flowmeter.

The maximum rate of ascent afforded by the pump is adequate for all purposes; 40,000 ft. (12.2 km.) is reached in five and a half minutes, 70,000 ft. (21.3 km.) in twelve and a half minutes, and 90,000 ft. (27.4 km.) in thirty minutes, while the descent from 90,000 ft. can be made in twelve minutes.

A special feature of the chamber is the extraordinary silence of operation. The pump and motor are housed about 20 ft. away in a sound-insulated room, with provision for avoiding the propagation of sound from the pump along the suction pipe, so that in the room where the chamber is situated all that can be heard while the pump is in operation is a low hum. In the chamber is a loose table, in shape a segment of a circle, which can be removed if desired to make room for bulky apparatus, such as a bicycle ergometer, for which there is ample room.

The oxygen supply for persons in the chamber is not built-in, but provided by means of the standard Service apparatus as used in aircraft, which has already been described, as also the oxygen cylinder outside the chamber for emergency use and the

short tubes in the wall of the chamber through which an additional supply can be piped in suitable packing if this should ever be necessary.

All respiratory physiology is based on the fundamental work of the great masters of the past and present, notably Paul Bert, Haldane, and Barcroft, and their schools, to whose writings grateful acknowledgment is due; because this approach to the subject was made from a purely practical standpoint, however, some of the theories here advanced were independently conceived in regrettable ignorance of the fact

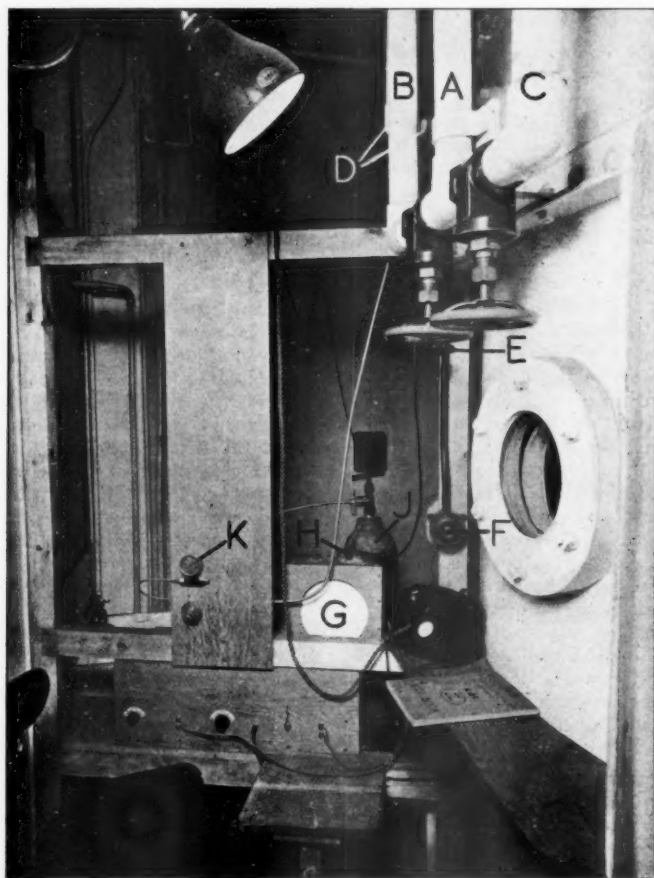


FIG. 5.—Decompression chamber, controls. A, suction pipe to pump; B, suction pipe from outer air; C, suction pipe from chamber; D, independent pipe to outer air and to oxygen cylinder; E, valve controlling D; F, button for stopping pump; G, microphone-loud-speaker; H, change-over switch for G; J, oxygen cylinder for emergency use; K, oxygen pressure-gauge.

(Crown copyright reserved.)

that they were not original. Acknowledgment is due also to the Chief Superintendent, Royal Aircraft Establishment, for constant help, to Sir Robert Davis, managing director of Messrs. Siebe, Gorman & Co., Ltd., for permission to show the pressure suit, and to the proprietors of *The Aeroplane*, for the loan of photographs.

Section of Neurology

President—C. M. HINDS HOWELL, M.D.

[March 18, 1937]

DISCUSSION ON THE NEUROLOGICAL SEQUELÆ OF SPINAL ANÆSTHESIA

Dr. Macdonald Critchley: The problem of nervous complications of spinal anæsthesia is one which well deserves ventilation by this Section. With few exceptions, the previous communications on this subject have been made by non-neurological writers, and the present state of the problem is still muddled and bereft of exact data, clinical and anatomical. In the present circumstances we are quite unable even to state how often neurological complications occur. The figures available are astonishingly contradictory; some surgeons or anæsthetists will tell us of thousands of successful cases without a single complication, while another writer (Blatt), is able to collect from the literature and elsewhere, evidence of 100 cases of 6th-nerve palsy after spinal anæsthesia.

I suggest that if any one point of certainty emerges from this discussion it will be the fact that a very significant number of nervous sequelæ are completely overlooked by both surgeons and anæsthetists. This statement will apply chiefly, I think, to the cases of ocular palsy and to the syndromes of the cauda equina and conus medullaris, which together, I submit, constitute the more common of the sequelæ.

Clinically, the neurological complications display great diversity and range from cranial nerve palsies to cases of polyneuritis. The meagreness of our pathological information renders any scientific classification impossible. This is the objection to Howard Jones' division of the nervous sequelæ into (1) the infective, (2) the traumatic, and (3) the toxic. G. H. Hyslop has grouped the nervous sequelæ according to whether they are of a focal or a general character, the former being subdivided into the remote and the adjacent types. Although this classification is not without value, it can scarcely be regarded as entirely satisfactory. Until a more logical schema becomes possible it might be equally useful merely to describe the neurological syndromes in their approximate order of frequency.

Headache.—This symptom occurs so often as scarcely to warrant its inclusion among the true neurological complications. It appears to develop with greater frequency than after simple lumbar puncture, and is especially common in cases of high block. The difficult question of lumbar-puncture headaches, their pathogenesis and avoidance, does not fall within the scope of to-night's discussion. One may say that headaches after spinal anæsthesia seem to differ from the post-puncture headaches in their greater frequency, in a greater liability to a severe and protracted course, and in the occasional development of complicating features, such as meningism or cranial-nerve palsies. The views of those practising spinal anæsthesia as to the causation of the headaches have been strikingly diverse, the blame extending from a faulty technique at the hands of the anæsthetist, to a neurosis on the part of the patient.

Aseptic meningitis following spinal anæsthesia has been recorded by S. Brock, A. Bell, and C. Davison in the same way as it has been reported very occasionally as a complication of simple lumbar puncture.

Abducens palsy.—Paralysis of the 6th nerve constitutes, according to the literature

at least, the commonest nervous complication. Actually, however, I have seen only two such cases :—

Case I.—Male, aged 62, developed a very severe headache after a planocaine anaesthesia. On the ninth day after operation, the patient noticed double vision in looking to either side. When examining him on the seventeenth day I found that there was now diplopia on left lateral ocular deviation only, due to weakness of the left 6th nerve.

Case II.—Male, aged 50, developed a severe headache for three or four days after a heavy stovaine anaesthetic. Diplopia appeared on about the fourth day. A month later the medical officer reported paralysis of the right 6th nerve, though six weeks after the operation, the left external rectus was found to be the only defective eye-muscle.

These two cases are typical in that the paralysis developed some days after the anaesthetic, in association with severe headache. In both cases the ocular paresis was probably bilateral, though unilateral cases have more often been recorded. Some of Fawcett's cases were accompanied by photophobia, dizziness, hallucinations, and tetanic contractions, as well as by headache. The lesion is usually transient and clears up in the course of a few days to months.

We are completely ignorant as to the pathogenesis of this complication. Cushing's hypothesis of brain-stem oedema with compression of the 6th nerve between the basi-occiput and a distorted anterior inferior cerebellar artery, is often assumed here, though entirely without evidence. We do not even know whether a condition of intracranial hypertension exists or not when headache and 6th-nerve palsy follow a spinal anaesthetic, though it would be a simple matter to measure the cerebrospinal fluid pressure manometrically.

Other cranial nerve palsies have been occasionally recorded after spinal anaesthesia. Nystagmus has been reported by E. Palestini and J. L. de Courcy. N. Jacqueau has described optic atrophy. Paralysis of the 7th, 8th, and 9th cranial nerves has been observed by C. Angelescu and S. Tzovaru. Other writers have at times recorded lesions of the trigeminal, facial, auditory, and hypoglossal nerves.

LESIONS OF THE CAUDA EQUINA AND CONUS MEDULLARIS

This type of sequel has proved in my experience the most common, though less frequently recorded in the literature. The syndrome is one which might easily be overlooked, especially when represented chiefly by urinary retention and sacral analgesia. The following are some characteristic cases :—

Case III.—Male, aged 69, noticed diplopia on the third day after a spinal anaesthetic. This persisted on and off for fourteen days only, but was followed by difficulty in micturition with impaired feeling of the passage of the stream of urine. There was no defect of rectal control or sensibility. The sole neurological abnormalities consisted in absence of the right abdominal responses and of the bulbo-cavernosus reflex, together with an extensor plantar response on the right side.

Case IV.—Male, aged 68, developed retention of urine after a spinal anaesthetic. The patient died eleven months later from his pre-operative condition, but the retention of urine persisted.

Case V.—Female. Developed immediately after a spinal anaesthesia numbness of the perineum and loss of bladder and rectal control. All her neurological symptoms cleared up within four weeks of the operation.

Case VI.—Male, aged 74, had a leg amputated under stovaine anaesthesia. After the operation retention of urine and faeces, and numbness of the remaining leg were noted. A large trophic sore developed in the heel, and the patient died from septic absorption and uraemia four months later. Urinary incontinence, which followed the state of retention, persisted up to the time of death.

Case VII.—Male, aged 40, had a leg amputated under planocaine anaesthesia. Thereafter retention of urine and foot drop were noticed. Knee- and ankle-jerks were unobtainable on the remaining limb, the plantar response being extensor. Later the knee-jerk returned.

sensation was impaired over the outer side of the calf and leg. Flexion and extension at the ankle-joint were almost impossible. These abnormal signs, together with difficulty in micturition and defaecation, were present when the patient was examined ten months later.

Case VIII.—Male, aged 62, immediately after a planocaine anaesthesia, developed retention, followed by incontinence, of urine and feces. Sores developed over the buttocks, and examination showed a flaccid paraplegia with absence of knee- and ankle-jerks as well as of the plantar responses. The blood Wassermann reaction and Kahn test were strongly positive. The patient died seven weeks later.

Case IX.—Male, aged 63, had his leg amputated under stovaine anaesthesia. Following the operation he noticed numbness in the bottom of the seat and in the urethra and bowel, so that he was unable to feel the passage of urine and feces. Double incontinence followed a period of urinary retention. Examination on the ninth day showed absence of the right ankle-jerk, with anaesthesia of the perineum. The patient has stated that he is then able to feel slightly the passage of a catheter.

Case X.—Male, aged 62, developed double incontinence after stovaine anaesthesia, together with oedema of the scrotum. Examination one month later revealed sluggish ankle-jerks with reduction of vibratory sense at the malleoli. Sphincter control was regained between the eighth and ninth week after the operation.

Although the particulars are not complete in these eight cases, nevertheless there is strong presumptive evidence of a lesion situated in the terminal portions of the spinal cord and roots. Two and possibly three of these eight cases showed some clinical evidences of improvement within a few weeks; in four others however symptoms persisted, without aggravation, up to the time of death. The morbid anatomy is unknown to me. The onset of symptoms immediately after the anaesthesia with no trace of subsequent progression suggests an acute toxi-infective process. The correspondence of the site of presumed lesion with the region of the cord influenced by the spinal anaesthetic, suggests a noxious effect upon the cord and its roots directly due to the anaesthetizing substance.

Radiculomyelitis.—In a smaller group of cases there is evidence of a more widespread morbid process affecting the roots and cord at a higher level.

Case XI.—Male, aged 69. Some days after a spinal anaesthesia the legs became weak and insensitive, and awkwardness and numbness developed along the inner aspects of the arms. Symptoms progressed to a state of flaccid paraplegia but thereafter some improvement occurred. Examination five months later revealed absence of the abdominal responses, as well as of the knee- and ankle-jerks. Plantar reflexes were flexor. Dorsiflexion of both ankles was weak; there was some reduction to pinprick over the feet, vibration being normally felt. There was no incontinence.

Case XII.—Male, aged 51, found that his left leg did not recover as the spinal anaesthetic wore off. For three days the left leg was powerless and when he was discharged on the nineteenth day he was still limping on that leg. This disorder did not clear up and when examined 2½ years afterwards he was still complaining of pains, weakness and numbness of the left leg which tended to swell at times. There were no sphincter disturbances but sexual potency was impaired. Examination showed ¾ in. of wasting around the left calf, with weakness of the whole limb. The knee- and ankle-jerks were absent on the left side; the left lower abdominal and the left cremasteric response were unobtainable and a flexor plantar reflex was obtained with some difficulty. There was marked thermal analgesia over the whole of the left leg and lower abdomen as high as the 11th thoracic segment, and vibration was much diminished at the left ankle.

I have notes of other rather similar paralytic cases, but the records are too brief to warrant quotation.

I have had no personal experience of cases of transverse, diffuse, or ascending myelitis. Cases of such are on record however. In the fifth case reported by Brock *et al.* a toxic myelopathy followed the use of a spinal anaesthetic. Autopsy revealed apparent softening of the cord at the 12th thoracic and 1st lumbar levels. Over a wider longitudinal extent there were found changes in the myelin sheaths, axis

cylinders and glia, most marked at the periphery and also at the root-entry zones.

Nonne and Demme have also reported degenerative myelitis as a sequel of spinal anaesthesia. Devraigne, Suzor, and Laennec, in the previous year, also described a quadriplegia of transient duration.

In a patient described briefly by Langton Hewer a myelitis developed after percaïne anaesthesia. Nine months later a laminectomy was performed, revealing a constricting zone of arachnoiditis around the lower part of the spinal cord and the upper portion of the cauda equina.

Anæsthetic areas of the body may be the site of complicating trophic disorders including, of course, severe bed sores. Hyslop has described two cases in which an herpetiform eruption appeared over the lumbar dermatomes after spinal anaesthesia, and Piccardi has mentioned two cases of vesicular eruption on the heels after tutocain anaesthesia.

Permanent neurological sequelæ need not necessarily be present, however, for extensive trophic lesions to appear, as shown in the next case :—

Case XIII.—Female, aged 59, became critically ill after a spinal anaesthetic. She remembers very little of the events of the next two weeks but recalls that the legs were stone cold. Blisters appeared on both thighs and on the right foot, gradually spreading so as to become gangrenous. There were no signs of neurological disorder.

It is possible that in this patient—who showed well-marked cardiovascular disease with degenerate peripheral arteries—a thrombosis in the vessels of the lower limbs may have been the immediate sequel of the spinal anaesthetic, which was in turn complicated by a spreading gangrene.

Sacral radiculitis.—In the following case symptoms suggestive of this diagnosis developed twenty-four days after a spinal anaesthetic :—

Case XIV.—Male, aged 46, had some persistent low backache after a spinal anaesthetic. He left hospital after three weeks and three days later, after a walk, he began to suffer from spasms of pain in the sacrum, groins and testicles. These were so severe as to throw him to the ground, the abdominal muscles being rigid and the spine arched in opisthotonos. Examination revealed no defect of the reflexes or of motor power; the sphincters were healthy; there was hyperæsthesia to all forms of cutaneous sensibility over the 2nd, 3rd and 4th sacral segments.

There are comparable cases in the literature, some of them diagnosed as examples of radiculitis and others of neuritis. Indeed, pains in the extremities have been regarded by some, e.g. Lindemüller, as constituting the commonest sequel. In three of this author's cases pain in the legs persisted for several months and was associated with marked and protracted tenderness of the muscles. Loeser reported five cases of limb-pains following a spinal anaesthetic within a period of one to three weeks. In three cases the upper extremities were involved, and in two the lower. The early symptoms comprised pain and paræsthesiæ affecting chiefly the territory of a single nerve, either motor or sensory. As a rule, the symptoms improved gradually after the course of many months, the nerves remaining tender to pressure and tension during that time.

Tabanellis has also reported a case of a spinal anaesthetic complication where the picture suggested a lesion of the brachial plexus.

Focal cerebral lesions.—In the next case, mental symptoms and a transient hemiplegia immediately followed a spinal anaesthetic.

Case XV.—Female, aged 68, a diabetic, developed a flaccid right-sided hemiplegia and aphasia some hours after an operation for which spinal anaesthesia had been employed. These symptoms cleared up in a few hours, leaving, however, a condition of mental confusion for some days.

The most probable explanation of such a case is I suppose a cerebral angiospasm or a small thrombosis, due in part to an associated vascular disease. Other cases of

hemiplegia following spinal anæsthesia have been recorded, for instance, by Arnheim and Mage.

Symptoms of neurological disease, precipitated by spinal anæsthesia.—It is not uncommon to find the first clinical manifestations of some clearly defined nervous disorder dating from a severe trauma, operation, or confinement. Spinal anæsthesia may also be a precipitating agent in the evolution of such affections as disseminated sclerosis, progressive muscular atrophy, and neurosyphilis. Examples of this happening in the case of each of these disorders have come to my notice :—

Case XVI.—Male, aged 28. Some years previously had been liable to attacks of giddiness. These improved to such a degree that he was able to join the regular army and also to get married. Three weeks after his marriage he underwent an operation for internal derangement of the knee-joint at a Military Hospital. On the third day after this operation, which was performed under spinal anæsthesia, he developed a retrobulbar optic neuritis in the left eye. Vision was practically abolished for six months. When examined two years later the visual acuity was still only $\frac{6}{60}$ in that eye, and other physical signs were present, typical of disseminated sclerosis.

The two cases recorded by MacLachlan of disseminated encephalomyelitis following spinal anæsthesia may also be examples of an independent neurological affection, where the symptoms were precipitated by the stovaine. His cases might also be instances of disseminated sclerosis.

Case XVII.—Male, aged 45, was well prior to an operation under spinal anæsthesia four years previously. Three months after, he developed weakness, pain and wasting in the left leg. Slowly the affection spread to the right shoulder and thence to the right leg. When examined four years later, he showed wasting and fibrillation of the muscles of both legs and to a lesser degree of both arms. The tendon-jerks were unobtainable and the plantar responses flexor. There were no sensory changes; no sphincter disorders and no bulbar signs. The patient still complained of pains which were practically generalized.

In this case the diagnosis is rather uncertain, though a progressive muscular atrophy seems the most probable.

Experimental work.—I may remind this Section that there is clear experimental proof of the toxicity of cocaine derivatives when injected intrathecally. Wossildo found changes in the nerve-cells up to twenty-four hours after subarachnoid injection of procaine in rabbits and dogs, though Pitkin's studies were not confirmatory of this. Changes had also been reported by van Lier. Spielmeyer, after injecting stovaine in dogs, found degeneration in the roots and peripheral zone of the cord with retrograde changes in the anterior horn cells. More recently, Loyal Davis, Haven, Givens, and Emmett, after injecting a series of common anæsthetic substances into the subdural sacs of dogs found (i) various inflammatory reactions in the leptomeninges; (ii) cellular changes in the grey matter of the cord recalling a retrograde degeneration; (iii) swelling and pigmentation of the axis cylinders; (iv) degeneration of the fibre-tracts within the cord. Of these changes the first were the most constant; the last three changes were less pronounced in those animals allowed to survive ninety days after the anæsthetic.

It would now be foolish to ignore the accumulating evidence that spinal anæsthesia may at times be followed by neurological sequelæ which, always disturbing in character, may even prove disastrous, if not fatal.

The most serious feature in this problem is that no steps can yet be taken to avoid these nervous sequelæ, for we are still ignorant as to their causation. This subject is therefore a very suitable one for discussion, especially among neurologists, anæsthetists, and pathologists.

Are some or any of these sequelæ attributable to faulty technique? to lack of skill in performing the actual puncture of the theca? to errors in dosage? to unsuitable pre- or post-anæsthetic medication or nursing? How far is the drop in blood-pressure a factor, by producing changes in the cerebrospinal blood circulation?

What part is played by the anæsthetic substance itself, and are nervous sequelæ commoner with one preparation than another ?

These are considerations which require an interchange of opinions by those with wide experience of spinal anæsthesia.

Furthermore, can it be that some or all of these nervous sequelæ are due merely to the activation of a latent morbid process within the nervous system by the spinal puncture or the anæsthetic ?

For permission to examine and quote the foregoing clinical cases, I am very grateful to numerous friends and colleagues, and also to Sir F. Kay Menzies in the case of patients within London County Council Hospitals.

Dr. J. K. Hasler: The giving of a spinal anæsthetic calls for two separate manœuvres on the part of the anæsthetist. Firstly, a lumbar puncture must be performed and, secondly, a drug must be injected into the canal and allowed to come into contact with a sufficient number of nerves to produce the required anæsthesia. Both these procedures may give rise to sequelæ, and I propose to discuss various points in technique which appear to me to be important in this connexion.

Let us consider first the lumbar puncture. This is, I am convinced, responsible for the majority of headaches which follow spinal anæsthesia and which can be such a source of annoyance to the patient. It has been suggested from time to time that the headache is due to the drug injected. If this were so, we should still require an explanation of those headaches which occur after lumbar puncture performed for diagnostic purposes. It is widely believed that the headache is due to leakage of cerebrospinal fluid through the puncture hole of the needle. Certain precautions should therefore be taken to prevent this. Firstly, the needle used should be as fine as possible. At least one observer has published results after using needles of two different sizes and has shown that with the finer needle the percentage of headaches is lower. I myself have been able to confirm this. In using a very fine needle of size 23 by the standard wire gauge it is necessary to have an outer needle with which to get down to the dura mater and through this is passed the fine needle to make the actual puncture. I have used one of these for several years now and I have sometimes found that on withdrawal of the inner needle cerebrospinal fluid leaks through the outer one although its point is not inside the dura. With even a fine puncture, therefore, some leakage can occur.

Secondly, the needle used should be properly sharp; any needle with a blunt or bent point should be discarded, to avoid tearing the dura mater. It should also be inserted gently, so that in the event of touching bone the point is not damaged. If the needle has a stylette, the stylette should be withdrawn before reaching the dura mater, so that the moment of puncture is known and the risk of blunting the needle against the anterior wall of the canal is avoided. I prefer also to make my injection in the middle line rather than from one side, as I believe it is easier to avoid bone in this way. Labat has suggested that the puncture should be made with the bevel of the needle in the long axis of the body, that is to say, in the line of the fibres of the dura mater. In this way a finer hole is made than if the bevel lies transversely to the fibres. I usually employ this technique but I am a little doubtful whether it makes any difference. In the prevention and treatment of headache it is usual to keep the patient in the Trendelenburg position on his return to bed. Any leakage that might occur can be prevented in this way because the puncture-hole then lies at the top of the column of fluid in the spinal canal. This fact can be demonstrated by performing lumbar puncture with a patient in the knee-elbow position. Although the point of the needle lies within the spinal canal, no fluid will flow out unless the patient is made to give a cough or his position is so altered that his head becomes higher than his lumbar region. Headaches may be due to infection which has been introduced into the canal by the needle. Aseptic technique is, of course, essential.

The second complication of the lumbar puncture which I wish to consider is gross damage to nervous tissue, caused by the needle. The spinal cord ends, in the adult, at the level of the first lumbar vertebra; in children and young adults it is at a lower level. If the needle is inserted at too high a level there is a very real danger of sticking its point into the cord itself with unfortunate results. In my opinion the needle should never be inserted above the third lumbar vertebra, and if for any reason it is found difficult to enter the space between L3-L4 then a trial should be made in the space below rather than in the space above. The failure to enter a space and the desire to try another space above, are usually the mark of an inexperienced operator. The failure is the result of a faulty approach to a space and can usually be remedied by inserting the needle at a point a few millimetres higher or lower than the original puncture-hole in the skin. Increasing practice in performing lumbar puncture leads to fewer failures and one is forced to the conclusion that one's early failures to enter a space were due to imperfect technique. It occasionally happens that when one is making a puncture the patient feels a shooting pain down a leg. I have always found this due to a lateral deviation of the point of the needle and it does not occur if the needle is kept strictly in the middle line. I have never seen harm come of it, but it is conceivable that a puncture made rapidly and with force might damage a nerve. In any case it is disconcerting to the patient and should be avoided.

A third complication of lumbar puncture is hæmorrhage. However carefully one may make the puncture, there always seem to be a few cases in which a blood-vessel is injured and blood flows from the needle. In most cases the flow of cerebro-spinal fluid soon washes away the blood and one can proceed to inject the anæsthetic solution. If not, the position of the needle is changed until one does get clear fluid. But the problem of the injured vessel remains. Is it likely to produce an extradural hæmatoma with possible pressure effects on the cord or nerves? or, if the hæmorrhage takes place intrathecally, will it give rise to adhesions with possible nervous sequelæ at some later date? These are points on which I should welcome information from members of this Section. So far as I am aware I have never had trouble following hæmorrhage when doing a lumbar puncture, but if a nervous lesion developed after the patient had left hospital he would seek advice elsewhere and I should be ignorant of it. I should therefore like to know whether any real risk is attached to hæmorrhage.

Let us consider now the second manœuvre in the production of spinal anæsthesia, namely, the injection of the anæsthetic solution. This solution has for its object the temporary paralysis—i.e. for an hour or two—of those nerves which supply the area of operation, after which the effect should wear off and the patient's nerves should function as before. Unfortunately, cases occur in which recovery is delayed or, as happens in a few cases, does not occur at all. In my own experience the commonest sequela has been interference with the nervous mechanism of the bladder, leading to retention of urine. Another factor, however, must be considered in this connexion, namely the nature of the operation. Retention is relatively common after operations on the rectum, irrespective of the form of anæsthesia used but, on the other hand, I do not remember to have seen a case of retention following urinary operations performed under spinal anæsthesia. While it is easy to see a connexion between a spinal anæsthetic and the subsequent permanent paralysis of one or more of the nerves which were acted upon, it is more difficult to see how a nerve at a distance can become paralysed. I refer to those ocular palsies which sometimes follow spinal anæsthesia. I have only once seen such a case among my patients and I have never heard of the condition remaining permanent. In considering the part played by the anæsthetic in the production of nervous sequelæ, there are three points to consider. The first is the nature of the drug or drugs injected. With the exception of percaine, all the drugs used for spinal anæsthesia are synthetic compounds allied to cocaine. It has been found that their toxicity and anæsthetic properties are directly propor-

tional and that the most efficient anæsthetics are the most toxic, cocaine being at the head of the list. In the early days of spinal anaesthesia in this country the drug most commonly used was stovaine, and a condition known as stovaine tabes has been described, following the use of the drug. It is a condition about which I regret to say I know very little, but it seems possible that it was due not so much to the drug itself as to early faults in its method of use. So far as I know, nothing of the sort has been described following the more recent use of novocain and percaïne, but that may be due to improved technique in their administration. I once saw three or four cases of headache and rigors following the use of percaïne, but it was in the very early days of percaïne anaesthesia when the drug had to be prepared in the dispensary, and I feel that there must have been some fault in its preparation as nothing of the kind has occurred since. There are at present on the market two solutions for spinal anaesthesia which, in addition to novocain as the anæsthetic, contain alcohol, which has been added to make the solution light. Now alcohol is a poison and is introduced into the spinal canal both here and in America with the idea of paralysing certain sensory nerves in cases of inoperable malignant disease in the pelvis. I have recently heard of one case in which this has also led to retention of urine and paralysis of the anal sphincter, therefore I view its use in spinal anaesthesia with some suspicion and feel that it is introducing an unnecessary risk into the proceeding. Sodium chloride and glucose are also used with spinal anæsthetics but I regard them as harmless.

[Next I wish to consider the possible effects that concentration and distribution may have in producing nervous sequelæ. If a drug, when used in a dilute form, has the effect of temporarily paralysing a nerve then the same drug, if used in greater concentration, may easily turn a temporary paralysis into a permanent one.] Some work has been done on this problem by Lundy at the Mayo Clinic. He administered concentrated solutions of procaine into the spinal canals of dogs and found that permanent paralysis resulted when 5 c.c. of a 20% solution was used, but that with 5 c.c. of a 17½% solution or weaker strengths no permanent paralysis occurred. What seems rather curious is the fact that no permanent paralysis occurred with 2.5 c.c. of a 50% solution. These concentrations are greatly in excess of those normally used in the human subject, though I believe there is a solution on the market in the United States in which the concentration of novocain is 40%. Except when using the dilute percaïne solution, it is customary to introduce a small quantity of the anæsthetic solution into the canal and allow it to flow along the canal, thereby spreading over a wide area and becoming diluted with cerebrospinal fluid. [It may occasionally happen, however, that if the injection is made with the patient in the sitting position, the anæsthetic solution becomes confined to that portion of the canal below the promontory of the sacrum. This is due to delay in getting the patient down into a horizontal position. Under these circumstances a low spinal anaesthesia will be produced and the few nerves that are paralysed will receive a stronger dose of the anæsthetic than if the solution had been allowed to cover a greater area. There are also those occasional cases in which, although the solution appears to have been injected correctly, yet anaesthesia is deficient except over a limited area, and one gets the impression that the solution has somehow been prevented from spreading—possibly by adhesions—and has remained in its relatively concentrated form in the vicinity of a few nerves. I mention these two sets of cases to show that it is possible, through faulty distribution, for nerves to receive a more concentrated dose of anæsthetic than was intended.] I have always thought that the solutions in common use were well within the safety limits as regards concentration but it might perhaps be better to give larger quantities of more dilute solutions, or to mix whatever solution we use with at least an equal quantity of cerebrospinal fluid before injection.

[Lastly, one must consider the possible effect of a spinal anæsthetic on those

patients who have an existing disease of the central nervous system. I am a little diffident of expressing an opinion on this point as I am in the presence of experts. Few anaesthetists would, I think, give a spinal anaesthetic to a patient who was known to have a disease of the central nervous system, but there must from time to time be patients in whom such a disease has not become evident and who are given a spinal anaesthetic. What effect, if any, will the anaesthetic have on the course of the disease? The point is of some importance because if the patient seeks advice at a later date, he may blame the anaesthetic for his disease.

I have tried to outline briefly those points in the technique of giving a spinal anaesthetic which appear important to me as an anaesthetist. If I have omitted any points which appear important to you, as neurologists, I hope I may be excused.

Dr. A. D. Macdonald: *Experimental and Pharmacological Considerations.*—I am neither a neurologist nor an anaesthetist, but have the good fortune, for a pharmacologist, to have a number of clinical colleagues who come to my laboratory to discuss their doubts and difficulties and subject their theories to experimental investigation. While I would be the last to suggest that we should blindly apply the findings on cats and dogs to man, I think that when faced with such problems as have been outlined by the opener of this discussion, we must explore every possibility of precise knowledge.

It would be unprofitable to attempt to review the published experimental work on spinal anaesthesia. Much of it is overwhelmingly conflicting, much is certainly erroneous in its conclusions. Instead I wish to summarize three pieces of joint research work which have been carried out in my laboratory—the first two inspired by a question of Dr. Falkner Hill's—"Why do spinal anaesthetics sometimes cause death on the table"—the last, which bears very directly on to-night's discussion, raised by Mr. Kenneth Watkins, "Why do we find bladder, rectum, and sensory disturbances persisting after spinal anaesthesia?" Two of these researches have not yet been published.

A glance at a skeleton of a cat or dog will show that lumbar puncture above or below the last lumbar vertebra should be easy, and with a little practice it is not difficult to tap clear cerebrospinal fluid. Because of the continuations from the cord into the tail, there is much less space than in man, but in our experiments we reject any in which a free flow of cerebrospinal fluid is not obtained, and any in which the fluid continued to be tinged with blood.

In the first place Dr. Bullock and I have tried to determine the fate of the injected drug—its spread in the cerebrospinal fluid, its dilution, absorption, destruction, and excretion. So far we have limited our work to drugs of the para-amino-benzoic acid series—procaine, larocaine, and tutocaine. These have the advantage of a reactive amino-group, and when coupled with guaiacol disulphonic acid yield an orange-coloured compound the concentration of which in cerebrospinal fluid, blood, urine, and tissues can be estimated colorimetrically to within 5%, although only small amounts are present. It is clearly important to make certain that the method is estimating the anaesthetic and not some derivative such as para-amino-benzoic acid itself. We have satisfied ourselves as regards concentrations persisting in the cerebrospinal fluid, by checking the colorimetric estimations with an assay against procaine, using the duration of anaesthesia produced by intracutaneous injections as a measure. A very good agreement was obtained.

Most anaesthetists who use procaine for spinal anaesthesia inject up to 3 c.c. of a 10% solution. Some dilute the drug further with cerebrospinal fluid before injection. In the cat 0.5 c.c. of a 10% solution may be injected without endangering respiration. This is about five times the full human dose, calculated on a basis of body-weight, yet it rarely affects the fore-limb tendon reflexes, though giving complete paralysis below that level for thirty to fifty minutes.

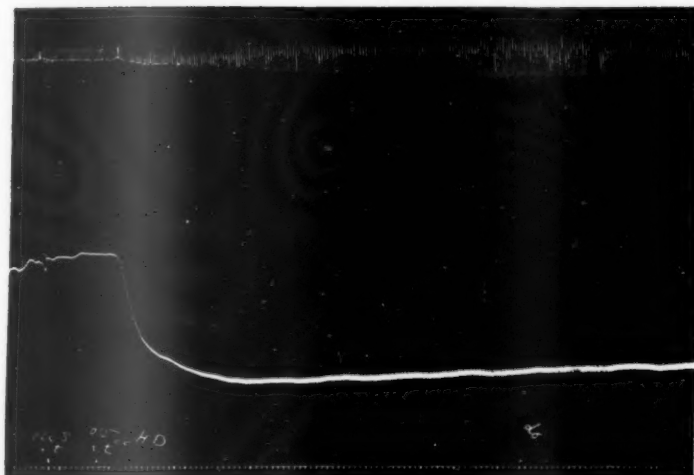
If small samples of cerebrospinal fluid are collected from the lumbar region at intervals and the drug content estimated, it is found that the concentration falls rapidly at first, then gradually. After five minutes it is usually between 2 and 3%. If a sample be taken at this stage from the cisterna magna, the concentration of drug there is surprisingly low—the highest we have found is 0.002%. One would not expect 6th-nerve palsies with such concentrations. After forty minutes or so, when the knee-jerk is back, the concentration in the lumbar region is usually below 0.05%. Larocaine and tutocaine are more potent and more toxic drugs, and give a longer anaesthesia after the injection of smaller doses. With larocaine the knee-jerk returns when the lumbar concentration has fallen to between 0.007 and 0.015%. With tutocaine the corresponding figures were 0.004 to 0.01%. (Slides showing the curves for the rate of disappearance of procaine, larocaine, and tutocaine from the lumbar cerebrospinal fluid.)

The concentration which is found in the blood at any time during or after spinal anaesthesia is low. It should not be necessary to-day to discount the fable that spinal anaesthesia may be dangerous because of the risk of blood absorption; both clinical and experimental evidence disprove it. Thus Hill has injected a full spinal anaesthetic dose of procaine hydrochloride, 300 mgm., intravenously in man, spreading the injection over a few minutes, without producing detectable symptoms, and Sebrechts has reported a similar experiment with percaïne. In the cat the liver may contain about twice as much as the blood; the concentration in the urine has never exceeded 0.03%, and only about 7% of the total injected is excreted by the kidneys—the rest is presumably broken down by the liver.

In our work on the acute effects of spinal anaesthesia (Hill and Macdonald [1933; 1935]) we gave repeated lumbar injections of 0.5 c.c. of a 10% solution of procaine. We had taken steps to prevent the drug from reaching the phrenic roots or respiratory centre by removing the spine of the 7th cervical vertebra and passing a drain round the cord. Only the first dose produced demonstrable effects. The respiratory tracing (fig. 1) is taken from the diaphragm, and with the injection the excursions recorded by the tambour are increased. This is because the intercostal muscles have been cut off by the spinal, the diaphragmatic movements increasing to compensate for the loss of thoracic movements. The blood-pressure falls abruptly with the spinal, but only to 70 mm. Hg. Later injections do not lower the blood-pressure further. We have found, in fact, that in the lightly anaesthetized cat this rather terrifying fall of blood-pressure does not occur if the injection be made slowly, so that there is time for compensating reflexes to make the necessary adjustments for the paralysis of the lower vasomotor roots. In most clinical cases, in which procaine is used, the anaesthetic in itself need not depress the blood-pressure.

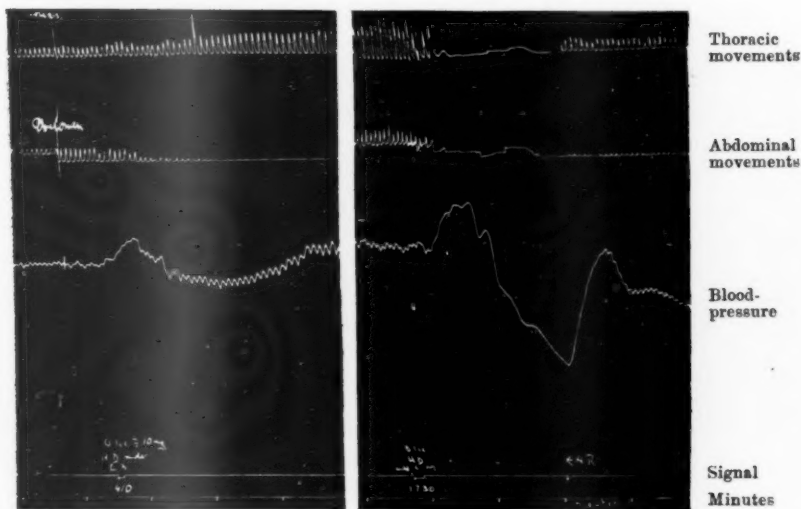
Here two respiratory tracings (fig. 2) are shown—the upper thoracic (intercostal), the lower abdominal (diaphragmatic). The injection (0.1 c.c. of 10% procaine) is first made at the level of the phrenic roots—between the third and fourth cervical vertebra. In contrast with the previous record, phrenic paralysis is produced, with compensatory increase in intercostal movements. Blood-pressure is little affected. For comparison, I have injected a similar dose into the cisterna magna of the same animal three hours later. This produces complete respiratory paralysis, the blood-pressure begins to fall, and the animal would perish were it not rescued by a few minutes of artificial respiration. In less than five minutes the depressed centre has recovered sufficiently from the effects of the drug to function independently.

Figure 3 is a more instructive tracing of a cisternal injection with respiratory paralysis, because the paralysis develops more gradually. There is a considerable rise of blood-pressure at first—a non-specific effect described by Dixon and attributed to stimulation of a suprarenal centre. The respiratory paralysis here is strikingly different from the phrenic paralysis seen in the last slide. Here the rhythm rather than the amplitude of the excursions is affected—the paralysis is central, not



[From the *Journ. Pharm. and Exp. Therap.*, 1933, **47**, 156.]

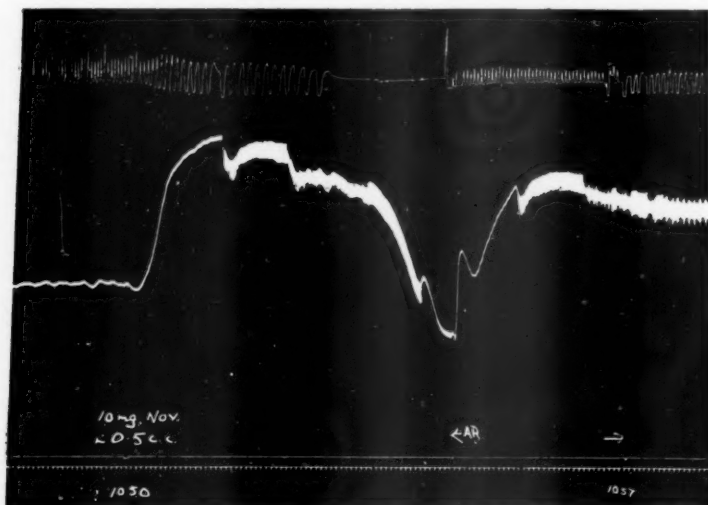
FIG. 1.—Lumbar injection. The time-tracings show intervals of five seconds. (In this and subsequent tracings the signal line represents zero blood-pressure.)



[From the *Journ. Pharm. and Exp. Therap.*, 1935, **53**, 459.]

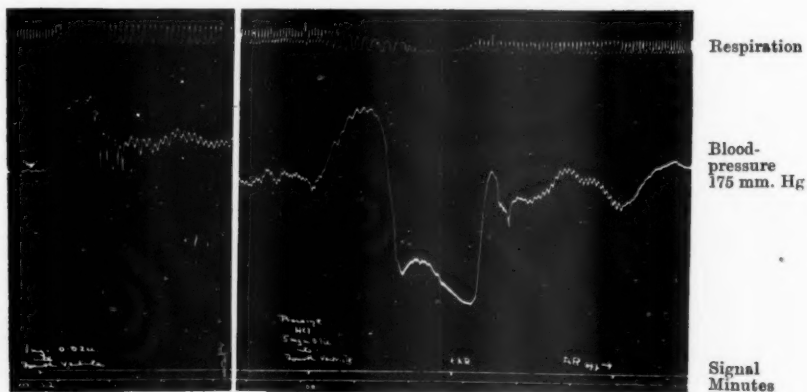
FIG. 2.—Cervical injection, and for comparison cisternal injection. The time-tracings show intervals of one minute.

peripheral, and every discharge from the centre, until it is paralysed, produces a full, deep respiration. Here again a very short spell of artificial respiration serves for the centre to recover its normal rhythmical activity.



[From the *Journ. Pharm. and Exp. Therap.*, 1933, **47**, 154.]

FIG. 3.—Cisternal injection. The time-tracings show intervals of five seconds.



[From the *Journ. Pharm. and Exp. Therap.*, 1935, **53**, 461.]

FIG. 4.—Ventricular injections. The time-tracings show intervals of one minute.

Here two injections into the fourth ventricle are recorded (fig. 4). After trephining and improving the access, the lower pole of the cerebellum is raised and a blunt hypodermic needle is passed up to the ventricle. With 1 mgm. of procaine, respiration

is slowed but not paralysed. With 5 mgm. a typical central paralysis, similar to those described with cisternal injections, is produced. Recovery with artificial respiration is rapid. The vasomotor disturbances associated with these central paralysees are transitory and not alarming—there is no evidence of any depression of the vasomotor centre similar to that of the respiratory centre.

So far, then, as we can judge from the experimental animal, the acute danger of spinal anaesthesia consists of the risk of headwards spread of the anaesthetic from the point of injection, depressing in turn the thoracic muscles, the diaphragm, and finally the respiratory centre. So long as it is possible to initiate and maintain adequate and timely artificial respiration, such paralysis does not seriously threaten the life of the animal. In avoiding respiratory paralysis, the important factor seems to be to limit the bulk of the injection—a voluminous dilute injection is much more likely to reach the phrenic roots or even the respiratory centre than an equal weight of drug in a more concentrated solution. But we shall see that a concentrated solution is not without its drawbacks.

When Watkins and I began our study of the neurological sequelae in the experimental animal, we realized that to obtain symptoms in a reasonable proportion of our animals heavy doses would have to be given. We began with $\frac{1}{2}$ c.c. doses of various 10% solutions of procaine—about five times the maximal clinical dose. In a fair proportion of animals this produces lasting symptoms—sensory disturbances, drooping of part of the tail, or complete flaccidity, paralysis of the urinary musculature with distension, so that urine could be expressed by abdominal pressure, the stream stopping as soon as the pressure was discontinued, rectal weakness with some protrusion of the mucosa through the anus, and occasionally some weakness of the hind limbs. Here we were concerned with the question—were these changes due entirely to the local anaesthetic, or to the presence of some other constituent of the solution such as alcohol or glycerine? A further possibility consists of some potentiation of the anaesthetic by such constituents. We satisfied ourselves that neither the alcohol nor the glycerine, in strengths greater than are commonly employed in proprietary solutions, produce sequelae in themselves. Further, since simple solutions of procaine may provoke lasting symptoms, it seems unnecessary to postulate some obscure potentiation.

Table I summarizes our results for several brands of procaine in 10% solution.

TABLE I.—SUMMARY OF EXPERIMENTAL RESULTS.

	Total	Normal	Paralysis	Percentage paralysis	Full	Tail only
Alcohol and glycerine (15 to 20% each)	23	23	—	—	—	—
"Heavy" duracaine (10% planocaine)	23	10	13	56	9	4
10% procaine (planocaine brand)	...	5	5	50	2	3
10% procaine (novocain brand)	...	23	17	26	4	2
5% stovaine (Barker)	...	10	4	60	—	6

We do not suggest that any significance should be attached to differences in the incidence of sequelae with the various procaine solutions, and it is interesting to find that 5% amylocaine (stovaine) seems to be as likely to leave sequelae as the stronger procaine solution.

After discussing these results with Dr. F. R. Ferguson we decided that we should try to correlate the incidence of sequelae with the concentration of the drug we had injected. That a correlation exists is clear from Table II. With $2\frac{1}{2}\%$, no symptoms

TABLE II.—RELATION OF DOSAGE TO INCIDENCE OF SYMPTOMS.
(Procaine hydrochloride)

Concentration (%)	Number of animals	Number showing some paralysis	Percentage paralysis
2.5	20	0	0
5	20	2	10
10	56	24	43
20	8	4	(80)
	(3 died acutely)		

appeared. With 5%, 2 of 20 cats had residual tail droop. The 10% injections are collected from Table I. I then tried a small series with 20%. The first two given 0.5 c.c. died in a few minutes, presumably from respiratory paralysis. I therefore reduced the dose to 0.3 c.c. or 0.4 c.c. according to body-weight, but lost another animal acutely. Of the five surviving, four showed considerable paralysis—weakness of the tail and hind limbs, some protrusion at the anus, and vesical dilatation. In this series simple procaine solutions were used, and the absence of prolonged changes with the weaker injections, sharply contrasted with their frequency with concentrated drug, is striking. This series provides further evidence that it is the local anæsthetic and not the other constituents of the solution or mechanical trauma due to the needle which provoke trouble. It would indeed be difficult to connect a prick of the cord or roots with the extensive symptoms sometimes seen.

We had at one time hoped to investigate the intrathecal morbid histology of the affected animals, but while realizing the importance and value of this line of work we are not at present prepared to discuss it.

In conclusion, if I may say a word about the experimentalist's outlook on the problems which Dr. Critchley has outlined, it seems to me that there are two pieces of well-established work that we should bear in mind. The first is Sherrington's proof that changes in the nervous system are more easily produced at the nerve-cells and synapse than in the actual nerve-fibre. The second is Gasser's proof that, of nerve-fibres, the smallest in cross-section are the most susceptible to the action of cocaine and its substitutes. These conclusions may help in evolving a satisfactory explanation of the phenomena under discussion.

[For permission to reproduce the tracings (figs. 1 to 4) the editors are indebted to the *Journal of Pharmacology and Experimental Therapeutics*.]

REFERENCES

- HILL, E. F., and MACDONALD, A. D. (1933), *J. Pharmacol. and Exper. Therap.*, **47**, 151.
Id. (1935), *Ibid.*, **53**, 454.
MACDONALD, A. D., and WATKINS, K. H., in press.

Dr. Fergus R. Ferguson: Despite the fact that I am bringing forward several rather disastrous complications, this contribution is not presented as a disparagement of a very valuable, if not indispensable, form of anæsthesia, but rather in the hope that as the result of inquiry, we may obviate such unfortunate and similar accidents in the future, and in order to emphasize the necessity for looking for and recognizing complications.

I stress this point because one has the impression that symptoms—such as paræsthesiæ, and sphincter disturbances and signs—such as sacral sensory loss and alteration in the tendon reflexes—resulting from lesions in the lower part of the vertebral canal and occurring as post-operative complications, are frequently overlooked. We all know the nurse who tells the patient who has an operation—say on the leg—and who says she cannot pass urine, that “she is not trying”, or if she is incontinent of faeces—that “she is careless”, or if she complains of numbness of her gluteal region, “what do you expect after an operation?”

In Manchester we have been unfortunate (or in another respect fortunate) in seeing numerous sequelæ during the past few years—epilepsy, persistent headache, 6th-nerve palsy, &c., but particularly cord symptoms. It is my intention to restrict my remarks to the lesions in the region of the cauda equina.

In the eighteen months' period between August 1933 and March 1935 we encountered 13 similar neurological sequelæ of spinal anæsthesia. These patients have been examined neurologically shortly after operation and on numerous occasions since. In addition Mr. Kenneth Watkins, who was R.S.O. at the Manchester Royal Infirmary when these complications were first noticed, has made many careful urological observa-

tions on these patients and has reported his findings in a paper which he read before the Association of Surgeons of Great Britain and Ireland.

One of the striking features is the large number of these cases over a relatively short period, for in a survey of the literature only about 16 similar cases—roughly the same number as we have seen ourselves—have been found. Dr. W. E. Paul, however, many years ago recorded details of two precisely similar cases—in the first the operation took place in 1913 in the Massachusetts General Hospital. His conclusions were that “spinal anaesthesia was not absolutely free from risk of damage to the lower sacral nerve supply and that the site and character of the lesion were matters for ingenious speculation”.

Unfortunately, nearly twenty-five years afterwards, we are in much the same quandary.

It is not my intention to record these cases in detail to-night, but the following are their main features:—

Period	...	August 1933 to March 1935.
Sex	...	11 males, 2 females.
Age	...	Average 42. Range 17 to 70.
Operations	...	Urgency 8: Perforated duodenal or gastric ulcer, acute appendicitis or cholecystitis.
	...	Others 5: Chronic appendicitis, intestinal obstruction, enlarged prostate.
Anæsthetic	...	Heavy duracaine (one ? stovaine).
Severity	...	8 severe, 5 mild.
Deaths	...	8.

In this list we note:—(1) The short total period—only eighteen months. (2) The preponderance of males (approximately equal numbers operated on). (3) Any age (excluding arterial disease as of importance). (4) All the severe cases occurred in the urgencies. The level of anaesthesia was higher than was required for some of the quiet cases, but there were two abdominal sections in the mild series. (5) The anaesthetic in all but one case was heavy duracaine and in the doubtful instance was in all probability heavy duracaine, but we cannot make absolutely certain. It might have been stovaine. (6) There were three deaths but in none of the cases could death be attributed directly to the spinal anaesthetic. In all three the operation was for a perforated duodenal ulcer. One patient died ten days after operation following a severe hæmatemesis—there was a litre of blood in the stomach. The second died about a month after operation from general peritonitis. The third died about four months after operation, with advanced pulmonary tuberculosis and a recent perforation of a tuberculous ulcer in the ileum.

Outlined below are the chief symptoms and signs contrasted in a mild and a severe type, although it is clear from examination of all these cases that the basic lesion was the same—the various patients showing different shades or degrees of the same syndrome.

	Mild type	Severe type
Reflexes:		Loss of ankle-jerks. Diminution or loss of knee-jerks.
	Diminution or absence of ankle-jerks.	
	Normal.	
Sensation:		Loss to P.P., H. and C., C.W., S.2.3.4.5.
	Subjective—numbness.	
	Sensory loss P.P., H. and C., C.W. in S.3.4.5.	
Micturition:		Retention, incontinence for six months. Frequency for two years.
	Difficulty or retention.	
Defæcation:		Incontinence of faeces for five months.
	Patulous sphincter.	
	Slight incontinence of faeces.	
	Unable to tell when flatus is being passed.	
	Loss of the normal sensation prior to bowel movement.	

The six slides exhibited (not reproduced) show the increasing degree of affection—from mild to severe cases—of the reflexes and area of sensory affection; broadly speaking there was a similar degree of increase in affection of one or both sphincters.

The bladder symptoms nearly always followed within twenty-four hours of the operation, whereas rectal symptoms were sometimes delayed—in one case for ten days—almost suggesting a progressive lesion.

In reviewing this series of graded cases it seems clear from the universal presence of some symptoms that the risk of affection was greatest to those roots of the cauda equina which were in the immediate vicinity of the site at which the drug was injected. Before it reached the more distant roots the concentration had been considerably reduced by admixture with the cerebrospinal fluid.

Despite the fact that these symptoms and signs may not appear striking, yet the importance of the problem is illustrated by the length of time the symptoms continue. The table below shows the progress of four of these patients—whom I have re-examined completely during the past fortnight (the first three being in the mild group).

Operation	PROGRESS.	
	Off work	Present state
1. W. E., two years ago. Chronic appendicitis.	Three months.	Very constipated; patulous anus. Sacral sensory loss. Loss of sexual power six months. Incontinence of faeces frequently. Frequency of micturition. Sacral sensory loss.
2. F. H., three years ago. Chronic obstruction.	Six months.	Very constipated. Sacral sensory loss with trophic ulcer. Passes urine hourly during the night. Slight sensory loss. Bowels normal.
3. A. W., two and a half years ago. Hallux valgus.	Eight months.	
4. G. D. J., two years ago. Perforated gastric ulcer.	Nine months.	

Patient 3 is interesting in respect of the mode of production of her trophic ulcer. Two months ago she married and she and her husband bought a tandem. The result is that in her attempts to pedal at the same rate as her husband she has worn quite a large hole in her sacral anæsthetic area. Another patient operated on two years ago, who was unable to come up for examination, wrote apologizing and said that he could not yet control his motions and his water was always running from him.

How much more devastating and lasting are these sequelæ than the majority of the post-anæsthetic chest complications!

Now as to some of the points in the causation and situation of the lesion. First, from the occurrence of these complications immediately after the anæsthetic and from the similarity to these accidents, it is certain that we must regard them as due to the spinal anæsthetic. We find it impossible to dissociate "heavy duracaine" from this particular group of complications, but we find it very difficult to say which is the particular factor which has caused these disasters. During the period under review about 1,000 heavy duracaine and 1,000 stovaine and other spinal anæsthetics were given. It has been argued that, if the anæsthetic is the cause and a satisfactory spinal anæsthesia has been produced, why are only a few nerves affected. Surely this is due to the fact that the maximum affection was on certain nerves—that is the anæsthetic came into contact with them originally in greater concentration or remained longer in contact with them.

Although it seems certain that the chief lesion in these cases is in the cauda equina, yet in view of the fact that spinal anæsthetic complications have been described affecting almost all parts of the nervous system and the difficult clinical differentiation from conus lesions, it is difficult to be dogmatic. Personally because of the large number of very similar cases in this series, I feel that we are probably dealing with a local toxic complication—something a little different from the more commonly recorded spinal anæsthetic neurological complication.

The part played by trauma.—It has always seemed to me to be impossible that a series of complications as illustrated by this group could be due to trauma—either direct puncture of a nerve or secondary to hæmorrhage either subarachnoid or subdural—yet there are still intelligent adherents of the traumatic view. First, surely

we must leave out of account those in which a high puncture has been carried out, for there is a large group where this point does not arise and yet the same complicating picture has been presented. In practically all these cases, the puncture was between the 3rd and 4th or 4th and 5th lumbar spines.

What are the points which make one feel so strongly about the part played by trauma?—for it is obviously a most important point and one on which we ought to come to a decision.

(1) Tens of thousands of "diagnostic" lumbar punctures have been made (some of them with much trauma) without any similar complication. There may be pain in the back or legs or headache, but never sphincter complications or loss of the leg tendon reflexes.

(2) There has been no evidence of bleeding into the cerebrospinal fluid in many of the patients, who have later shown complications.

(3) The lesion is too extensive to be regarded as due to puncture of one, two, or even three, nerves.

(4) The punctures in cases showing complications afterwards may be absolutely clean and straightforward. In the last example we saw, the technique was described as perfect.

(5) The grading of the cases in this series—variations of one lesion; it seems impossible to reconcile this state of affairs with injury either to a nerve or to hæmorrhage.

(6) The same grading is seen in Macdonald's recent experiments, in which, irrespective of the type of puncture, he was able to produce graded increasing nerve affection by increasing the concentration. Surely this could only be due to the effect of a "toxic" or injurious substance introduced into the cerebrospinal fluid.

(7) The post-mortem and experimental evidence suggests a toxic affection, but no evidence of any hæmorrhage even in a careful post-mortem examination within a week.

(8) The necessity for correlating the lesions in the lower cord, upper cord, and 6th-nerve palsies with the local ones in the sacral cord and cauda equina.

When driven into a corner, the "traumatic protagonist" says that during the puncture a nerve may be pricked and then the "anæsthetic" does the damage at this site, or that the injection was partly extradural. Granting these possibilities, surely it would be impossible to produce such extensive lesions.

On all counts then, it would seem to be impossible to regard the actual puncture as being the cause of these sequelæ. It must then be the anæsthetic. The fact that complications have been recorded after *stovaine* and *novocain* seems to suggest that the *novocain* compound is the toxic agent.

[But why was this large series encountered after heavy *duracaine*? We must turn to the other constituents of this preparation. Its composition has varied—but *glycerine*, *gladine*, *gum acacia*, or *alcohol* seem to be the possible culprits.

Naturally *alcohol* fell under great suspicion. Certainly *alcohol* may produce a lesion of this type; *Kafer*, *Pereyra*, and *Sanguinetti* have recorded an identical lesion following injection of 80% *alcohol* and containing 25% *antipyrine*. There seem to be several reasons on the other hand, for believing that *alcohol* is not the direct cause.

(1) That similar spinal complications have followed clinically and experimentally anæsthetics without *alcohol*, e.g. *stovaine*.

(2) That 90% *alcohol* has on occasion been introduced intrathecally in doses of 1 to 2 c.c. without causing any complications. In *Queen Square* recently a patient received over 3 c.c. of 90% *alcohol* intrathecally in three doses over a period of a few days but no definite abnormality was found on careful examination.

(3) According to *Dogliotti*, intrathecal injections of absolute *alcohol* into dogs only caused motor paralysis of a few days' duration.

(4) Professors Macdonald and Watkins were not able to produce paralysis in cats by the intrathecal injection of 15% ethyl alcohol with 20% glycerine.

It does not seem possible then that the lesion can be due directly to the alcohol and/or glycerine.

The composition of heavy duracaine has varied, and complications have followed when no gliadine or gum acacia has been present. It was introduced in order to allow of slow diffusion of the anæsthetic solution into the cerebrospinal fluid and thus allow the anæsthetic to act on the intradural nerve-roots at chosen levels.

I would suggest that it was the combination of the procaine with the alcohol and glycerine and the gum acacia which led to the undiluted procaine being held too long locally in contact with the nervous tissue close to the site of the injection and therefore being allowed to exert a local toxic affection in susceptible persons. One feels that the glycerine was probably the most important factor in producing this effect.

In conclusion then with particular reference to these "cauda equina complications" in this series one cannot but feel (1) That heavy duracaine in average hands is a dangerous spinal anæsthetic and should not be used in its present form. Naturally in the Manchester Royal Infirmary heavy duracaine is now only given in a very small number of cases and during the past two years there has been only one definite cauda equina complication which has come to my notice (and this was due to heavy duracaine). (2) That in order to keep the concentration at which the procaine preparation first comes into contact with nerve tissue, as low as possible: (a) the preparation should be diluted with cerebrospinal fluid (at least an equal quantity); (b) that the injection should be made slowly.

Dr. Russell Brain said that this discussion afforded an opportunity to pool experiences in regard to these interesting, but fortunately rare, complications of spinal anæsthesia. He therefore wished, first, to mention among cranial nerve palsies that of a case which he had seen in which both 6th, both 7th, and both 8th nerves were affected, but the patient recovered completely in two weeks. And he had seen two or three cases of unilateral 6th-nerve paralysis.

Dr. Critchley had pointed out how rare it was to find records of adequate pathological investigations of the conditions which had been described this evening, and for that reason Dr. Dorothy Russell and himself were taking this opportunity of putting on record a case which he would describe as one of myelomalacia following the administration of a spinal anæsthetic.

MYELOMALACIA FOLLOWING SPINAL ANÆSTHESIA

The patient was a man, aged 33, a pastrycook. Apart from bronchitis during the previous three years his general health had been good. He was admitted to hospital on account of a displaced right semilunar cartilage and on September 3, 1934, this was operated on under a spinal anæsthetic. The anæsthetic used was spinocain, of which 2 c.c. were injected after lumbar puncture between the 3rd and 4th lumbar vertebræ. He had no symptoms until a week after the operation, when he complained of pain in the lumbosacral region of the spine. He made a good recovery from the operation, however, and was discharged from hospital, walking, on September 15. Towards the end of September, nearly a month after the operation, he began to have pain in the left knee and increasing difficulty in walking. He had to go to bed, and a feeling of numbness developed in the left foot and gradually spread up the leg. At the same time the right leg became weak and the pain in the back increased, so that he had difficulty in turning in bed. This pain spread upwards and became severe and gripping round the waist. He was readmitted to hospital on October 24 and on that date developed retention of urine.

I examined him first on November 8. The fundi, pupils, and cranial nerves were normal. In the upper limbs there was slight symmetrical wasting of the

small muscles of the hands, with moderate weakness of movement most marked in the deltoids, triceps, and extensors of the wrists. The right supinator jerk was absent; the left was present but sluggish. The remaining tendon reflexes of the upper limbs were normal and there was no sensory loss. The intercostal muscles contracted normally. There was marked weakness of flexion of the spine on the hips and the patient was unable to sit up unaided. The abdominal reflexes were absent. In the lower limbs there was moderate wasting of all muscles which was least marked in the hamstrings and most marked in the peronei and anterior tibial group and was symmetrical. There was bilateral foot-drop and almost complete flaccid palsy of both lower limbs except for an extremely feeble movement of flexion and extension of the right hip. The knee- and ankle-jerks were absent and the plantar responses were a very feeble flexor. There was slight impairment of appreciation of light touch over the dorsum of both feet and considerable loss of sensibility to pin-prick over all the sacral-segmental areas. There was gross loss of postural sensibility in the toes of both feet and the vibration of a tuning fork was not appreciated over the feet or the left shin but was felt over the right shin. There was retention of urine and obstinate constipation. Lumbar puncture on October 30 yielded the following results: Protein 0.270%, globulin ++, no excess of cells, Wassermann reaction negative. Subsequently there was no change in the patient's neurological condition and he died on December 24, 1934, from complicating infection. Pathological examination, which Dr. Russell will describe in detail, showed a massive softening of the spinal cord, maximal at the level of the upper part of the lumbar enlargement.

A review of the literature has revealed very few cases of this kind and fewer still which have been investigated pathologically. Brock, Bell, and Davison described a similar case, the seventh of their series. A point of special interest in our case is the long latent interval before symptoms appeared, pain in the back occurring a week after the anaesthetic and motor symptoms not until nearly a month after. In two of Brock, Bell, and Davison's series of eight cases the neurological complications appeared when a second spinal anaesthetic was given, in one case twelve days and in the other case thirty-seven days after a first. They raise the question of whether the neurological sequel may not be due to some process of sensitization. With this in mind and in view of the fact that spinocain contains gliadin, a wheat protein, and our patient was a pastrycook exposed to wheat flour, we asked Professor Marrack to sensitize three rabbits with gliadin and we subsequently injected spinocain intraspinally. There were no ill-effects, but the injections were difficult, and we feel that no conclusion can be drawn from the experiment. In any case the fact that neurological sequelae have followed the administration of other spinal anaesthetics not containing gliadin or other protein makes it probable that the anaesthetic drug itself is in some way responsible. In this case, however, the long latent interval between the administration of the anaesthetic and the development of symptoms makes it difficult to regard the symptoms as the direct result of the drug. The interval may have been the incubation period of a process of sensitization, and in these days one must mention the possibility of a superimposed virus infection, though the pathological changes do not appear to support such a view.

Reference.—BROCK, S., BELL, A., and DAVISON, C. (1936), *J.A.M.A.*, **106**, 441.

Dr. Dorothy Russell : (Pathological Report).

Macroscopic examination (P.M. 563/1933. *Appendix*).—The brain, spinal cord, and a segment of sciatic and of musculo-spiral nerve were received after fixation in formaldehyde. The spinal cord alone presented visible changes. On account of the complete absence of the spinal dura and of the terminal part of the cauda equina the accuracy of the segmental levels given in the following description is doubtful.

There was brownish-grey discoloration and extreme softening of the lower part of the 12th thoracic segment, which extended caudally to the upper part of the 2nd lumbar segment. Below this level the discoloration and softening gradually diminished. The pia over the posterior surface of the sacral segments was occupied by a plaque (1.5 cm. from above down by 0.6 cm. from side to side) of opaque grey exudate. Apart from this there was no macroscopic evidence of meningitis. A series of transverse sections showed an opacity of the posterior columns, which was confined to the tract of Goll in the cervical segments. A few punctiform hæmorrhages were present in the grey matter at different levels. In the 10th to 11th thoracic segments there was a diffuse creamy-white opacity of the whole of the white matter, the borders of the grey matter being obscured. This showed a gradual transition caudally into the brown pultaceous softening described above, and the cord became too soft to cut until the 3rd lumbar segment was reached. In the remainder of the lumbar segments the cord was still very soft and showed a central diffuse light-brown discoloration fading to yellowish-brown at the periphery. A dark reddish-brown streak occupied the ventral fissure. In the 1st sacral segment the centre of the cord was replaced by a dusky brown area of softening; a V-shaped opaque creamy-yellow area occupied the left posterior horn, the two arms of the V radiating from the central softening. The posterior columns were translucent and grey, the rest of the white matter milky-white. In the more caudal sacral segments there was an area of hæmorrhagic softening in the posterior columns, which gradually diminished to the size of a pinhead in the 3rd segment.

Microscopic examination.—No histological changes were found in the central nervous system above the level of the medulla oblongata. Excessive softening precluded examination of the 12th thoracic segment and of the upper part of the lumbar enlargement. Sections of the 3rd and 5th lumbar segments show complete necrosis of the grey, and almost complete necrosis of the white, matter. Only occasional myelin sheaths are seen here and there in Loyez preparations and most of the glial cells have been destroyed; a few pyknotic nuclei are seen and there is a sparse infiltration with degenerating polymorphonuclear leucocytes throughout. Slight diffuse hæmorrhage, apparently of recent origin, is present in the posterior columns of both these lumbar segments and in a few peri-vascular zones in other parts of the white matter in the 5th. No bacteria are present in sections stained by carbol-thionin blue and by neutral red and the Weigert-Gram method. Meningitis is limited to an uneven, mainly perivascular infiltration with lymphocytes, monocytes, and a moderate number of both neutrophil and eosinophil leucocytes (figs. 1 and 2). Conspicuous collections of foam-cells are present at the junctions of the anterior and posterior roots with the cord and elsewhere in an interrupted zone immediately beneath the pia.

The most striking histological changes, however, are those present in the pial blood-vessels (fig. 1) and in the small perforating arterioles in the periphery of the cord (figs. 2 and 3). Both the medium-sized and smaller arterioles have undergone partial or complete hyaline necrosis which gives a positive reaction for fibrin. Necrosis is accompanied by hæmorrhage into the walls and into the adventitial spaces. They frequently show thrombosis and, in some instances, early organization of the thrombus. The anterior and posterior spinal arteries, however, are unaltered, except over the 5th lumbar segment where each posterior spinal artery contains a crescentic mass of unorganized thrombus, while its medial and adventitial coats are infiltrated with lymphocytes, monocytes, neutrophil and eosinophil leucocytes. There is endophlebitis of many of the larger pial veins, the infiltrating cells being mainly lymphocytes and plasma cells.

In the 1st and 2nd sacral segments there is necrosis of the posterior columns, associated with hæmorrhages. A dense compact zone of fat-granule cells, stained bright orange-red with Scharlach R, occupies the cord at the borders of the necrotic

area (fig. 4). In Hortega preparations the fat-granule cells are seen to be of microglial origin because many transitional forms of these cells are present nearby. The adventitial sheaths of neighbouring vessels are infiltrated with plasma cells and lymphocytes. Discrete foci of demyelination and ballooning of the medullary

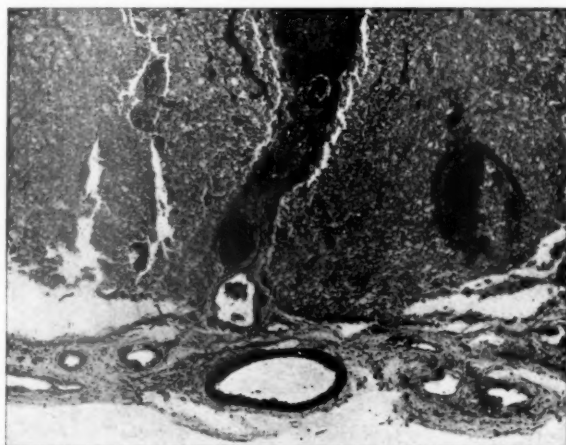


FIG. 1.—Anterior fissure of fifth lumbar segment, showing thrombosis of central branch of anterior spinal artery. Hematoxylin and eosin. $\times 38$.

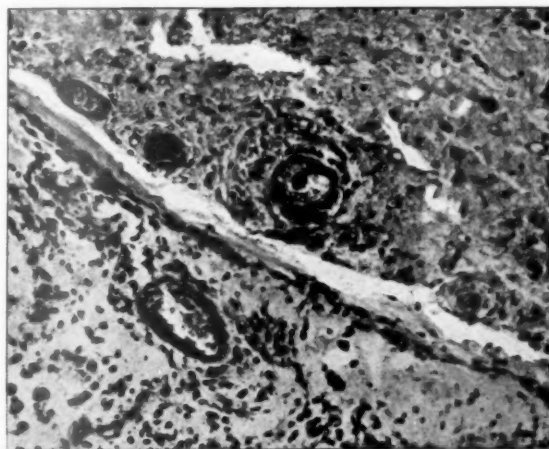


FIG. 2.—Margin of lateral column of fifth lumbar segment, showing necrosis, thrombosis and perivascular hemorrhage affecting small vessels. Inflammatory reaction in adjacent pia. Hematoxylin and eosin. $\times 150$.

sheaths, presenting a fenestrated or honeycombed appearance, are also present in the lateral and anterior columns; they are not obviously related to blood-vessels. The pia is sparsely infiltrated with lymphocytes and plasma cells. The arteries and arterioles of the pia are normal, but endophlebitis is present in the larger veins.

At higher levels of the cord the histological changes are less intense. In the 11th thoracic segment there is a patchy, symmetrical demyelination and ballooning of the sheaths in peripheral parts of the white matter in the lateral, and, to a less extent, in the anterior and posterior columns (fig. 5). These areas resemble the discrete

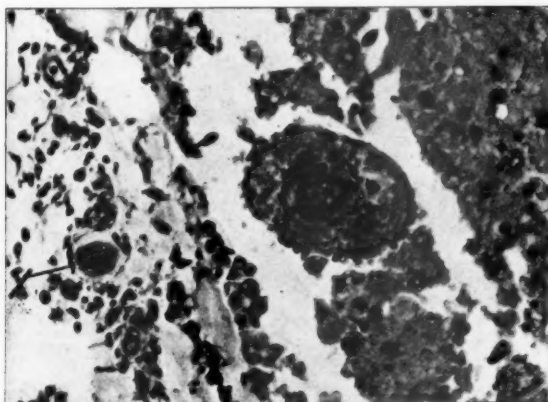


FIG. 3.—As in fig. 2. Another field showing necrosis of small perforating arteriole with extensive hæmorrhage in perivascular space. Note hyaline swelling of wall of smaller arteriole (x) in pia and great reduction of its lumen. Hæmatoxylin and eosin. $\times 190$.

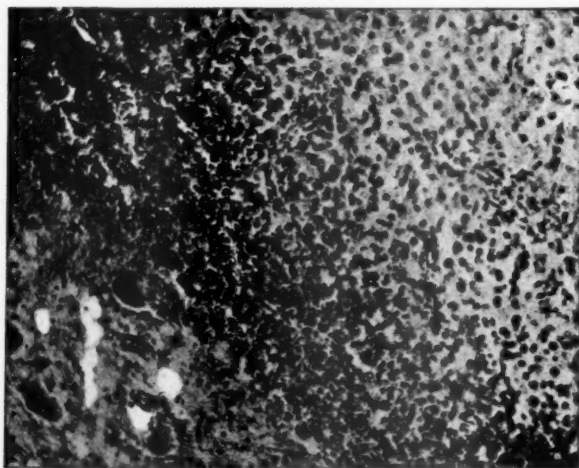


FIG. 4.—First sacral segment, showing dense zone of fat granule cells demarcating necrotic posterior columns (top right-hand corner) from grey matter of anterior horn (lower left-hand corner). Frozen section: Scharlach R and hæmatoxylin. $\times 92$.

foci described in the sacral cord. In Hortega preparations they contain foam cells; these give no reaction with Scharlach R but contain black granules after treatment with osmic acid (Marchi's method). The areas are possibly to be associated with

focal necrosis and thrombosis of the small perforating arterioles, because one thus affected vessel is present in the left lateral column. There is no meningitis. In Loyez preparations there is a partial diffuse loss of myelin sheaths in the posterior columns. Marchi preparations show a slight diffuse degeneration, the affected sheaths being most numerous in the ventral parts of the posterior columns. In the same segment severe degeneration of the anterior horn cells is shown by chromatolysis, margination of nuclei, and pyknosis.

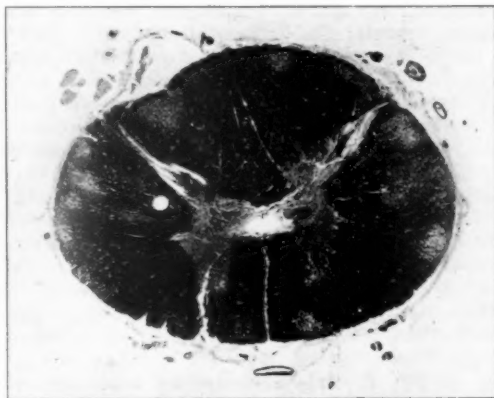


FIG. 5.—Eleventh thoracic segment, showing scattered foci of demyelination. Loyez hæmatoxylin. $\times 8.5$.



FIG. 6.—Second servical segment, showing partial loss of myelin in tracts of Goll. Loyez hæmatoxylin. $\times 8.5$.

Above the 11th thoracic segment the only histological abnormalities are a secondary ascending degeneration (fig. 6) and a few small recent hæmorrhages in the grey matter. The neurones are well preserved. All blood-vessels appear normal, except a small vein over the left posterior root in the 6th cervical segment, which contains partly organized thrombus.

The portions of peripheral nerve received for examination show no histological abnormality.

Comment.—The histological appearances do not suggest that there was any direct trauma to the spinal cord at the time of the anæsthetic; there is no evidence of old hæmorrhage; recent hæmorrhages are present but they are small and scattered. Nor is there any histological evidence indicative of bacterial infection at the time of the anæsthetic; the inflammatory reaction in the pia is scanty and of a chronic type; bacteria were not demonstrated histologically. The possibility that a virus was introduced at the time of giving the anæsthetic cannot be excluded, but the limitation of the reaction to the lowest segments of the cord is against this theory. The appearances suggest strongly that the massive softening in the lower thoracic and upper lumbar cord and the focal areas of demyelination in higher segments are secondary to the severe changes in the pial and perforating blood-vessels. In the affected areas veins show endophlebitis or thrombosis, while arteries show kinds of acute necrosis, or "necrotizing arteritis", which are identical with those most commonly found in periarteritis nodosa, some examples of nephritis, rheumatic fever, and massive cortical necrosis of the kidneys. Similar arterial changes have been caused experimentally by sensitization of animals to foreign proteins, bacteria, or filtrates of bacterial cultures (Vaübel, 1932; Metz, 1932; Apitz, 1933, 1934), and consequently the changes have been attributed to hypersensitization and have been called hyperallergic arteritis. They have also, however, occurred in the kidney of man in dioxan poisoning (De Navasquez, 1935), and Dr. F. B. Byrom (1937, *in the press*) has produced them in rats by injection of vasoconstrictors. In the absence of evidence, therefore, that spinocain has a direct necrosing effect upon arteries or causes vasoconstriction the most probable explanation of the destruction of the spinal cord in the present case would appear to be a hyperallergic arterial necrosis and endophlebitis. As Dr. Russell Brain, however, has pointed out above, it is difficult to accept this view, because of the fatal case of Brock, Bell, and Davison. In this case the clinical history and the pathological changes in the cord appear to have been similar, although no mention was made of abnormal vessels. But the anæsthetic used was percaine, which contains no protein, and only one injection was given, so that a sensitization appears to be excluded. It must be added, however, that in two out of six other cases reported by Brock, Bell, and Davison, symptoms of radiculitis appeared only after a second injection, and the authors said that these two cases did suggest sensitization.

REFERENCES

- APITZ, K. (1933), *Virchow's Arch. f. path. Anat.*, **289**, 46; (1934), *ibid.*, **293**, 1.
 METZ, W. (1932), *Beitr. z. path. Anat. u. z. allg. Path.*, **88**, 17.
 VAÜBEL, E. (1932), *ibid.*, **69**, 374.
 DE NAVASQUEZ, S. (1935), *J. Path. and Bact.*, **41**, 385.

Dr. H. K. Ashworth said that four years ago he had opened a discussion on this subject at a meeting of the Section of Anæsthetics.¹ The opening papers in the present discussion indicated that since then distinct progress had been made in clarifying knowledge concerning these undesirable sequelæ of spinal anæsthesia. From the point of view of the anæsthetist it was most desirable to divide the sequelæ into those which were definitely dangerous to the patient, and those whose sequelæ were more transient.

With regard to the dangerous category, no doubt the cauda equina lesions, described by Dr. Ferguson, should be in that group. Others which were a source of potential danger—mentioned by Dr. Critchley and others, were those in which the patient had incipient disease of the nervous system, which could not be detected beforehand and was precipitated into action or increased activity by the administration of a spinal anæsthetic. These cases would always be "fallen for" unless there was any detectable pre-warning of a nervous lesion.

¹ *Proc. Roy. Soc. Med.*, 1933, **26**, 581 (Sect. Anæsth. 19).

It was reasonable, as Dr. Ferguson had said, to presume that cauda equina lesions were directly connected with the use of small quantities of heavily concentrated solutions of drugs, together with the other solvent substances present, acting in the region of the site of injection. He asked if any member knew of a case of cauda equina lesion following the use of a 1:1,500 solution of percaïne given in bulk, because if there were frequent reports of cases in which these lesions occurred with a small concentrated dose of novocain derivatives, and were not found after a large injection of a very weak solution of percaïne, the evidence would be considered to be fairly conclusive as to the cause of these cauda equina lesions.

The more transient sequelæ of spinal anæsthesia—headache and 6th-nerve palsies were slightly more common after the use of 1:1,500 solution of percaïne than after the use of novocain solutions, and it was reasonable to suppose that this should be so, because a much greater volume of fluid was injected. He had given percaïne in about a thousand cases, and had had two cases of 6th-nerve palsy among them; both cleared up, although one of them took four months to do so. The more serious lesion, from the point of view of blame allotted by the patient, was headache. Neurologists usually saw only the severe cases of nervous sequelæ of spinal anæsthesia; from the anæsthetist's point of view, headache was much the commonest of such sequelæ. Here, neurologists and anæsthetists were on common ground, because headaches occurred after lumbar puncture. He himself had undergone lumbar puncture some time ago, and had had a severe headache afterwards; on the whole, he thought that it was a hypotension headache, as it was agony for him to sit up. He would very much like to hear of a cure for this type of headache.

With regard to the causation of headache: A German worker had recently published a paper on this subject, in which he analysed 2,000 cases of spinal anæsthesia, in 1,000 of which large needles were used, and in 1,000 very thin ones, and he did not find any difference in the incidence of headache in the two series. What he did find was a difference of incidence in the age-groups; on the whole the younger and more highly strung people were much more prone to headaches than were elderly ones, and this almost without reference to the kind of anæsthetic used. Moreover, patients who had been given spinal anæsthetics without their knowledge—preliminary evipan was often given in private practice—had developed headaches, therefore one could not accept the suggestion that these headaches were always functional. The German worker to whom he had alluded advocated the use of nitroglycerine as a cure. Shortly after reading the paper in question he (the speaker) had had two cases of headache following the use of percaïne, and in neither case did the use of nitroglycerine result in a cure.

Dr. Wilfred Harris said he was unable to accept Dr. Ferguson's theory that the pathological effect of concentrated novocain on the nerve-fibres of the cauda equina was due to its direct action on those fibres. For many years he (the speaker) had been accustomed to inject the sciatic nerve with novocain in a strength from 2% to 5%, without seeing any permanent damage result. A patient might complain of numbness, which might last from half an hour to an hour, and there might be anæsthesia and foot-drop which might last an hour; but nothing persisted longer than that time. If there were any damaging effect on the nerve-fibres in the cauda equina more constant symptoms should also be present in his sciatic cases. He thought the paralytic symptoms described were a sacro-myelitic effect, and he suggested that the cause of these sacro-myelitic accidents was a thrombotic, possibly vasoconstrictor, action of the novocain itself; its effect on the pial vessels might cause such symptoms and pathological results as Dr. Russell had demonstrated this evening.

Dr. Ferguson (in reply to Dr. Wilfred Harris) said that there was considerable difficulty, on clinical grounds, in being dogmatic about the exact situation of the lesion. He did not think there was sufficient evidence to enable one to say more than

that the lesion was in the region of the cauda equina. At first it was thought that the lesion was confined to the cauda equina itself, yet on reviewing the 13 cases, in order to bring them into line with the experimental findings and with other complications recorded in the lumbosacral region and other parts of the cord, one could not exclude the possibility of the lesion being in the conus medullaris or sacral cord. However, the localized affection in some of the patients, the absence of dissociated sensory loss in the anæsthetic areas, the diminution in calf tenderness, the mode of recovery, the site of the puncture, and the fact that cases of radiculitis following spinal anæsthesia had been described, seemed to be in favour of a lesion maximal in the cauda equina, despite the difficulty which Dr. Harris had mentioned. It seemed possible that the nerves forming the cauda equina were more sensitive to the anæsthetic than the sciatic nerve.

Autopsies had been performed on the three patients who died, but no definite abnormalities were found macroscopically. The sections of the cord showed some increased hyaline changes in the vessel walls and, in addition, some marginal pallor of the cord in the sacral region, but no other definite changes.

Marchi sections were negative. Dr. Susman, who examined the sections carefully, considered that the sacral nerves showed fine vacuolation and evidences of recent degeneration.

Dr. Purdon Martin, referring to the case described by Dr. Russell Brain and Dr. Dorothy Russell, said he had seen one case in which there occurred an ascending myelitis, and eventually encephalomyelitis, following spinal anæsthesia. The patient had, first of all, the usual symptoms of a sacral lesion and then numbness, which spread upwards; a week later he had symptoms of a high spinal lesion, and there were indications that this was rather worse in the cervical than in the dorsal region, and again worse in the lumbar region. A day or two after the high spinal manifestations the patient had hemiplegia on the right side, then on the left side, and he died. The post-mortem examination was carried out by Sir Bernard Spilsbury, who took away all the significant material, and he, Dr. Martin, had not heard the results of the more detailed examination.

Dr. Anthony Feiling (Chairman) said Dr. Ashworth had asked whether any member knew anything about complications of the nature under discussion occurring after procaine. Dr. Critchley had mentioned in his paper, a case recorded by Dr. Langton Hewer, in a man who had persistent paraplegia and was subsequently operated upon, the anæsthetic being procaine. And Mr. Dickson Wright had recorded two cases of temporary mania following the use of the same drug for local spinal anæsthesia.

Could Professor Macdonald tell members what was the effect of these anæsthetics on the spinal blood-vessels?

Professor Macdonald (in reply) said that, so far as he was aware, straight novocain itself had no action on the blood-vessels, and he would be surprised if a simple 5% solution of procaine produced extensive changes. Every student in his class carried out cutaneous tests, and he himself, with the collaboration of a dental friend, had done many tests on himself with a 2% solution of procaine. In the absence of adrenaline the effect was dilator rather than vasoconstrictor. A 10% solution was being used intrathecally by him, but he had no experience of such concentrations applied in other fields.

Section of Medicine

President—Sir CHARLTON BRISCOE, Bart., M.D.

[March 23, 1937]

DISCUSSION ON THE EFFECTS OF ASPHYXIATING GASES ON THE RESPIRATORY SYSTEM

Major Stuart Blackmore: I have no clinical experience in the subject of our discussion but I have worked in the Chemical Defence Research Station for some years, though my recent work has been more on the administrative side.

Ætiology.—I want to talk particularly about phosgene, because, though there is considerable difference of opinion on the military and air-force side as to whether, in the event of gas being used in future wars, lung irritants will be much used, or at all, yet there is no difference of opinion on the point that if they are used, phosgene is the most likely to be employed. On this subject of ætiology Müntsch (Berlin) says:

"Recent researches have shown that the theory accepted up to the present of a muriatic acid corrosion of lung alveoli does not furnish a completely satisfactory explanation of the origin of the lung œdema. It would be remarkable if the alveoli alone were attacked whilst the upper airways remained free; further, pure muriatic acid gas produces no lung œdema—to do this, a concentration 800 times stronger than phosgene would be necessary. Other theories assume reabsorption of the phosgene into the circulation, resulting in changes and softening of the brain, and finally, by way of the nervous system, a secondary origin of the lung œdema."

There is one suggestion concerning possible ætiology which I think a doubtful one, but I put it forward as a matter for consideration. Possibly we are dealing with some interference with the more domestic economy of the cell, some interference with oxidation and the reduction processes, or with the acid base equilibrium. I have no definite views to put forward on this, but I hope to hear it spoken of in the discussion. The ætiology of the subject is in every way unsatisfactory.

Take another lung irritant, chlorine; a member of the halogen series, all of which are irritant to tissues. It is not unreasonable to think that chlorine has a direct action, and the results are attributable to that action. It is astonishing in how many chemical warfare agents chlorine is present; in some it seems to be the deciding factor. Take mustard gas: if you substitute for chlorine any other radicle of the halogen group you find a reduction in the poisonous effect of the compound. Hence the chlorine itself seems to be of definite importance. Although chlorine is present in so many warfare gases, we do not know whether it is the compound, e.g. phosgene which is doing the damage, or the product of the disintegration of the molecule.

Pathology.—The effects of lung irritant gas poisons are demonstrated by changes which include œdema and alterations in the blood-vessels and blood-supply, and are associated with bronchial spasm. The œdema is the outstanding factor of importance from the pathological and the therapeutic points of view, and it is from the consequent lack of oxygen that the bad effects accrue.

Cases can be divided, generally, into two main groups, which are distinguished by their clinical appearance as either purple or blue, and grey. I show on the screen

colour-photographs of each. Underlying both types anoxæmia is the main defect, due to obstruction to the passage of oxygen into the blood-stream by the imposition of the layer of water around the alveoli. That is interesting, because the oedema is associated with variations between production and drainage. In the very early cases—I am speaking chiefly of phosgene—you will find that there is a thin layer of fluid inside and lying on the alveolar epithelium, before there is any oedema in the lung substance. At this time very little change in the lymphatic area is demonstrable. This thin layer of fluid is not enough to cause immediate results, and the person concerned is frequently unaware of any impairment of function at all. Yet there is already a deficiency of oxygen supply, and that is why it is, clinically, so vitally important that in all these lung irritant gas cases the patients should be treated, from the very first, with rest; they should not be allowed to take exercise, whether they do or do not feel ill, as this interference with the oxygen intake is already present, and an extra demand for oxygen resulting from exercise may cause sudden death.

When the condition advances further and there is oedema in the lung, there is a variation in the lymphatic supply, and the problem is one of balance between production of fluid and drainage. There is frequently such a heavy oedema that as much as one-fifth of the total fluid volume of the blood has been lost. A great amount of fluid is lost to the circulation by expectoration and by extravasation into the tissues—so much that there is a definite thickening of the blood in many cases. When we come to treatment I shall have something to say about that. If we have many of these cases to treat, as in air raids, it would be wise to arrange for some simple procedure, as in cholera cases, with glycerine-and-water bottles, to test the specific gravity and concentration of the blood, so that we may know when it is advisable to use an infusion.

I want to point out the difference between the lung irritant gassed case, and the lung affected by mustard gas. The condition in the mustard gas case is entirely different, for in that there is just inflammation—the effect of mustard gas being burning effect on the tissues, so that there is a different problem to meet; there is a damaged superficial area, which is very liable to bacterial invasion, but there is not the interference with the oxygen supply which I have mentioned, and which is due to the oedema in the previous kind of case.

In order to investigate the effects of lung irritant gases on the bronchioles, it is advisable, at autopsy, to tie the trachea before opening the chest. This prevents the simultaneous semi-collapse of both bronchioles and alveoli. In examination by this method it is seen that in lung irritant gas poisoning there are closed bronchioles and widely open alveoli. This largely explains the patchy distribution of the oedema, because if the bronchiole contracts sufficiently rapidly and completely to prevent the entry into the alveoli of the poison, then that area will escape from the oedema formation; whereas when the reverse occurs and there is no bronchial contraction there will be a full dose in the alveoli resulting in serious oedema production.

Treatment.—As regards anoxæmia, three factors are to be noted: firstly, the hindered absorption of oxygen from the alveoli; secondly, the obstruction of the blood-flow in the lung, due to an increased viscosity, with its ill-effects on an already anoxæmic heart; thirdly, actual bronchial obstruction. There can be no argument about the value of oxygen. These cases depend for their survival on continuous oxygen administration over many hours, sometimes days. It is clinically true that oxygen administration cannot begin too soon—with the proviso that the supply must be conserved. Secondly, the administration must not cease until the patient is either dead, or has reached the stage at which stoppage of oxygen administration for five minutes does not result in a clinical retrogression.

Now, what is the accessory treatment? Atropine is useless; indeed it is contra-indicated. Bleeding is definitely of value, and can hardly be carried out too early.

Later on the congested heart may be relieved by bleeding as practised clinically—but why early bleeding is of such marked value in these cases I do not feel sure. It has been suggested that by bleeding up to about 300 c.c. a reaction is produced in the opposite direction, and may indirectly reduce the oedema.

Next with regard to infusion. There is much discussion and difference of opinion in this matter. Vedder highly recommends infusion, and a variety of liquids are recommended for it: normal saline, hypertonic saline, glucose solution, and urease solution. The use of urease was suggested by the theory of poisoning by acid formation, because the effect of it is to produce ammonia from urea, thus neutralizing any acid produced. American workers advocate the introduction of urea as well as urease into the circulation as a treatment for this form of gas poisoning. English workers do not consider this treatment of much use. In America the use of emetine, with urea and urease, is recommended, with the hope of securing a lasting constriction of the capillaries so as to restrain the production of oedema and thus shield the individual from its bad effects for a long period. Of that I have no experience.

Dr. Ronald V. Christie said he agreed with Dr. Blackmore that surprisingly little work had been done in this country on the pathological and functional aspects of gas poisoning. He suggested that both the French and the English had been remiss in paying so little attention to the work of the Germans in this field. This German work was done for the most part under the auspices of the best physiologists and pathologists available and there appeared to be little excuse why their publications should be disregarded (Aschoff, Flury, Gildemeister, Heitzmann, Koch, Laqueur, Magnus, Mayer, Ricker, &c.—See Laqueur and Magnus 1921 and Flury 1925). For instance in 1920 and 1921 a series of articles was published on the action of phosgene. It was shown that amongst many other interesting observations on the functional impairment following phosgene poisoning, section of both vagus nerves in animals largely prevented the onset of the classical signs and symptoms. From a large and varied series of experiments these investigators concluded that the action of phosgene could be divided into two categories: (1) The irritant effect of the hydrochloric acid which is liberated as phosgene passes into solution. This irritation involved the whole respiratory tract and, in the concentrations used in gas warfare, could be of little importance. (2) The more direct effect of phosgene on the nerve-endings of the pulmonary vagus. It appeared that it is this action on the vagal nerve-endings which, after a latent period, led to the development of pulmonary oedema. So far as could be found in the literature, these experiments had never been refuted. Soon after the publication of this work, the German physiologists became particularly interested in the phenomenon of so-called "vagus pneumonia" (Weiser, 1932, &c.). The details of this phenomenon need not be discussed. It would suffice to say that certain disturbances of function of the pulmonary vagus led to the development of a patchy hæmorrhagic oedema of the lungs. The possible significance of this phenomenon with regard to the vagal theory of phosgene poisoning was obvious. If this theory was correct, a detailed survey ought to be made of the effect of parasympathetic drugs, and of various anæsthetics.

With regard to the dyspnoea of phosgene poisoning the textbooks showed a lack not only of attention to published work, but also of comprehension of well-known physiological principles. Dyspnoea was usually ascribed to the combination of anoxæmia and retention of carbon dioxide. Although the action of these two factors was usually assumed to be synergic, they could more conveniently be dealt with separately.

(a) *Anoxæmia*.—Uncomplicated anoxæmia did not cause dyspnoea. Two weeks previously a paper had been read at a meeting of the United Services Section¹ on

¹ G. Struan Marshall, *Proc. Roy. Soc. Med.*, 1937, **30**, 995 (United Serv. Sect., 9).

respiration while flying at high altitudes, in which the word dyspnoea had hardly been mentioned.

"The relatively slight increase in the amount of air breathed during very serious anoxæmia has frequently been lost sight of in the interpretation of clinical symptoms . . . In the very dangerous pure anoxæmia of high altitudes or carbon monoxide poisoning, increase in the breathing is not a prominent symptom" (Haldane and Priestley).

Furthermore, the available data on the effect of oxygen therapy on phosgene poisoning showed that, with the relief of anoxæmia, there was seldom any significant diminution in the respiratory rate.

(b) *Retention of carbon dioxide.*—Several investigators had shown that, except in the terminal asphyxial stages of phosgene poisoning, there was no retention of carbon dioxide. Indeed the tension of carbon dioxide in the arterial blood was usually below normal, except where death was imminent.

It could only be concluded that the dyspnoea of phosgene poisoning was due primarily neither to anoxæmia nor to carbon dioxide retention, nor to a combination of both. The true cause was not difficult to find. German authors had shown that the lung became more rigid and less distensible as the symptoms of phosgene poisoning developed. On theoretical grounds such a change should cause rapid and shallow breathing through the increased sensitivity of the Hering-Breuer reflex. That this was indeed the mechanism involved, had been shown by the observation that blocking the impulses through the vagus nerves abolished the rapid and shallow breathing.

The conception of dyspnoea as reflex, rather than chemical, in origin was of considerable practical importance. The relief rather of anoxæmia than of dyspnoea should be the criterion of success of oxygen therapy. It was true that, in those cases where pulmonary congestion was increased by heart failure, respiratory distress might be somewhat relieved by the administration of oxygen. This only applied to cases in which anoxæmia had already damaged the heart. Oxygen therapy should preferably be instituted before this myocardial damage had been done, and its administration should be continued whether or not there was any relief of dyspnoea.

With regard to the treatment of phosgene-poisoning by agents other than oxygen, he (Dr. Christie) suggested that the maintenance of a positive intra-alveolar pressure throughout the respiratory cycle might diminish the tendency to pulmonary oedema. It was claimed that pulmonary oedema of cardiac origin could be successfully treated by this method.

REFERENCES

- FLURY, F. (1925), "Handbuch der Normalen und Pathologischen Physiologie". II Band, Julius Springer, Berlin.
LAQUEUR, E. and MAGNUS, R. (1921), *Ztschr. f. d. ges. exper. Med.*, **13**, 31-179.
Id., *Ibid.*, 200-290.
WEISER, J. (1932), *Pflüger's Arch. f. d. ges. Physiol.*, **231**, 68.

Dr. Burton Wood said that after the Great War those who saw many ex-service men expected to find traces of gas-poisoning in the lungs. The effects which Dr. Blackmore had described were not those which might be expected to give rise to permanent pulmonary damage such as fibrosis. In the exhaustive report of the United States Army Council a good deal of attention was directed to interstitial pneumonia attributable to the action of mustard-gas or of secondary infection following it. Such results were illustrated. Now a very large number of ex-service men complained of lung trouble which they attributed to the War, and a very large proportion claimed to have been gassed. Yet one sought in vain for any evidence of the kind of fibrosis which resulted from interstitial pneumonia. Pneumonias of this type due to causes other than gas were well known, and their results were evident.

For example, he (the speaker) had recently seen a patient who had suffered from pneumonia complicating typhoid fever, and a skiagram of the chest had shown the lower lung fields heavily "cobwebbed" as the result of interstitial scarring. A similar condition might sometimes be seen after an incompletely resolved influenzal pneumonia. The fibrosis due to silicosis or asbestosis was clearly shown by X-rays. But he had seen nothing analogous in the chests of ex-service men, nor could he recall having seen a single example, in an ex-service man, of fibrosis resulting from gas poisoning. He asked Dr. Blackmore if there was any evidence that interstitial pneumonia due to gas action had left a permanent effect on the lungs. He himself favoured the view of Landis that gas poisoning was either rapidly fatal or followed by recovery practically complete.

Dr. Horace Evans, referring to the great importance of the administration of oxygen in the treatment of these cases, asked what method of administration Dr. Blackmore advocated.

Dr. C. W. J. Brasher inquired whether recent research had thrown any further light upon the mode of action of phosgene on the tissues? He related the case of two subalterns who were "gassed"—apparently slightly—with phosgene in 1915, when serving in Flanders. They were sent to a casualty clearing station, but were not detained. They were warned of the danger of exertion during the next few days. Three days later, feeling quite well, they walked up a slight ascent but, on reaching the summit, one of them fell to the ground and died immediately.

In view of the frequent occurrence of cyanosis and of severe symptoms of circulatory failure in these cases, was it not probable that phosgene was a protoplasmic poison that acts directly upon the alveolar cells (hence the early occurrence of acute pulmonary oedema), and also upon the cardiac muscle-fibres, to which it had been conveyed in the blood-plasma?

Major Blackmore (in reply) said he agreed that the French and British had rather dropped investigation on this subject, and he thought that was a pity. A disproportionate amount of attention had been given to the effects of mustard gas; it was important, but should not monopolize attention. Lung irritant gases were extremely dangerous war chemicals, and if they were successfully used, large numbers of cases would have to be dealt with.

With regard to interstitial pneumonia and fibrosis: These appearances were met with after mustard gas infection of the lungs, and here one was dealing with a very different pathological condition, and the bulk of the deaths from it were due to the septic pneumonia supervening on the burning effect of the vapour. In those who survived there were permanent after-effects, whether or not the lung was originally in a healthy condition. But one did not see serious after-effects in cases which could be proved to have been due to lung irritants only; here the dictum "death or complete recovery" seemed to be quite sound, provided the lungs were in a healthy condition before the poisoning was experienced. That was the conclusion arrived at by the Ministry of Pensions, after a carefully conducted statistical survey. If after-effects were found in this kind of case they were purely neurasthenic. This fact was particularly important in regard to tuberculosis; there was no evidence that tuberculosis arose more frequently in gassed people than in others, indeed the evidence was rather the other way, though it was not suggested that gassing was a preventive of tuberculosis.

So far as he knew, lumbar puncture had never been used in these cases. He did not see why it was likely to be of much use, but probably any active intervention of that kind, aimed at relieving pressure, might be of considerable advantage, and he

would remember the hint if it should be his misfortune to have to treat these distressing cases.

The idea that there was a general poisoning effect following phosgene was strenuously combated by all authorities. They attributed the cases of sudden death on exertion to the immediate effects, or the after-effects, of the anoxæmia; it did not appear that phosgene was a general protoplasmic poison.

As to the method of administration of oxygen, the two fundamental principles which had to be adhered to were: (1) Conservation of the oxygen supply, because it was so vital for these cases, and because procuring fresh supplies might be difficult; (2) its administration must be as nearly continuous as possible. The oxygen should be administered by apparatus like that of Haldane, which would collect the gas flowing from the cylinder during the period of expiration, and would not allow it to escape. It was usually suggested that a start should be made at a speed of 3 litres a minute, and if the immediate clinical improvement expected did not happen, the speed should be increased, but it should not exceed 10 litres a minute, as control experiments on normal persons showed that the normal rate of breathing and the normal diffusion-rate of the gas were such that no further increase in the proportion of oxygen in the alveolar air would occur if the initial supply were increased over that rate. One did not want an apparatus which would deliver pure oxygen, as that would act as an irritant to already irritated tissue. Interruption of oxygen administration for five minutes in every half-hour would give an idea as to whether or not more oxygen was required. Usually if a patient during the interval did not show retrogression it would be unnecessary to continue the oxygen, as he had probably turned the corner, unless intercurrent septic conditions or pneumonia supervened. But it might be necessary in some cases to administer oxygen in this way for many hours, even days. One patient, who eventually recovered, was under that routine for fourteen days, but such cases were rare. In most of the cases the patients were well on the road to recovery within the first forty-eight hours. Some 75% died in the first twenty-four hours, but the administrator must be prepared to carry on day and night under the steady routine described. The oxygen need not be warmed before being given.

Owing to the great amount of expectoration, vomiting, and dyspnoea, these cases were difficult to nurse.

Section of Comparative Medicine

President—GEORGE W. DUNKIN, M.R.C.V.S.

[March 24, 1937]

DISCUSSION ON NUTRITION AND ITS EFFECTS ON INFECTIOUS DISEASE

Dr. Stuart J. Cowell: It is notoriously difficult to establish the truth regarding the effect of individual hygienic factors on the health and well-being of mankind, one reason being that, in large-scale observations, it is virtually impossible to exclude the influence of factors other than the one which is being deliberately varied. While it is fairly generally agreed in the medical profession that some connexion exists between imperfect nutrition, or faulty feeding, and susceptibility to infectious disease, the actual evidence relating specific variations in diet to changes in resistance to definite types of infection is extremely conflicting.

There is no cause for complaint about the quantity of evidence on this subject, and only a fraction of the recent contributions can be referred to in this discussion. These contributions can be grouped in more or less distinct categories, and I propose to deal with some of the more important of them.

(1) *Attempts to correlate the incidence and course of infections with the characteristic diets employed by different races, social groups, or institutions.*

In this group would be included studies such as that of Nicholls, who in 1936 published a dietary survey of Ceylon and attempted to relate the effect of the very imperfect dietaries common among certain classes of the population to the distribution of the malaria epidemic which ravaged the country in 1933-34. His conclusion was that "even if the masses had been well-fed there would have been an epidemic—but the vicious cycle of malaria and destitution acting and reacting on one another would not have been established—the mortality rate would have been lower and convalescence would have been shorter". In the same group would be placed the observations of Orr and Gilks on the diets and health of the Masai and Kikuyu tribes in East Africa. There were far more admissions to hospital for bronchitis, tropical ulcer, and malaria among the latter, who subsisted largely on cereals, than among the Masai, who lived chiefly on meat, milk, and raw blood. Spence compared the incidence of such infections as bronchitis and pneumonia among poor and well-to-do children in Newcastle. Such infections were about eight times as common among the poor children, a great many of whom showed some evidence of being imperfectly fed. McGonigle, who has made similar studies in Stockton, did not find any close correlation between unsatisfactory diets and the incidence of bronchitis in children. The frequent occurrence of certain infections in institutions has been

studied in relation to possible dietary faults. Thus the high death-rate from dysentery in some prisons in East Africa a few years ago was apparently related in part to the very ill-balanced rations of the prisoners. A striking reduction in the mortality rate from this disease followed improvement of the dietaries. Rather similar observations have been reported from asylums in our own country.

In many of the studies belonging to this group it is difficult to decide how far bad diets alone were responsible for the increased incidence of infections, for obviously many racial, social, and other environmental factors must have varied, as well as dietary habits. Nevertheless, the evidence obtained along these lines does suggest that grossly defective diets diminish the resistance of human beings to certain kinds of infection.

(2) *Attempts to determine the effect on the incidence of infectious diseases of changes in the diets of a whole population or of an isolated section of a community.*

There seems a fair measure of agreement that the increased incidence of tuberculosis in Central European countries towards the end of the Great War was due at least in part to the severe quantitative and qualitative food restrictions which were imposed on the inhabitants. From time immemorial famine has been regarded as bringing pestilence closely in its train. On the other hand, the great influenza pandemic of 1918-19 appeared to ravage the comparatively well-fed troops as severely as the less well-fed civilian populations. The effects of less drastic dietary changes have been followed by Dr. Friend at Christ's Hospital. He could observe no clear relation between the dietary changes which he instituted in the school from time to time and the incidence of colds and febrile chills, though he did find an indication that septic infections of the skin were more common when the diets contained more sugar.

(3) *Attempts to define the part played by individual food constituents in determining resistance to infections.*

Many of the observations in this category have been made as the result of experimental work on laboratory animals. I propose to deal in turn with some of the evidence concerning the possible relation of the supply of individual vitamins and mineral elements to infections in man.

Vitamin A, which has been called the anti-infective vitamin, will be considered first. No one questions the fact that severe degrees of deficiency of this vitamin are practically always associated with bacterial invasion in all species of laboratory animals. Most observers who have studied vitamin-A deficiency in man on any large scale have also reported an increased susceptibility to certain kinds of infection. The question which has aroused the most attention in recent years, however, is whether a liberal supply of this vitamin confers increased resistance to infections on individuals who do not show obvious signs of this particular deficiency. Many studies have been published in which the incidence of special types of infection among individuals who have received some preparation of vitamin A or carotene has been compared with the incidence among a control group to whom the preparation has not been given. The duration of illness, the frequency of complications and, with serious infections, the death-rate, have also often been compared in such tests. In some studies the aim has been limited to determining the effect of large doses of vitamin A on the clinical course of established infections. These tests have, on the whole, yielded negative results. A positive result obtained on one occasion has usually been followed by a negative result obtained by a different set of observers studying the same kind of infection. Many series of observations have been reported in connexion with the common cold, perhaps with rather more positive than negative results. The incidence of puerperal infections and the course of puerperal fever have been studied in relation to the provision of extra supplies of vitamin A; again both positive and negative results have been obtained. Mortality rates from pneumonia have been studied in South Africa: in one series this vitamin seemed to

have exerted a distinctly favourable effect, while in another it was without any effect. The clinical course of measles in fever hospitals has been the subject of two investigations in our own country in recent years. In the first it appeared that a concentrate of vitamins A and D was responsible for a significant reduction in the mortality rate. In the second test, carried out in much the same way, no reduction in the mortality rate was found in the group which had been given the supplement of vitamins A and D. In the only two investigations on this subject with which I personally have been concerned, negative results were obtained. One was concerned with the effect of a vitamin-A concentrate on the winter sickness rate of Royal Air Force recruits and the other with the effect of the same concentrate on the occurrence of otitis media as a complication of scarlet fever.

Such results cannot be interpreted as proof that vitamin A plays no part in determining the resistance of human beings to infections, but they do suggest that no dramatic effects are to be expected as the result of giving supplements of vitamin A to those whose diets may already contain a sufficiency.

It has been much debated whether vitamin D is concerned with maintaining the resistance of human beings to infections. Clinicians have for a very long time stressed the tendency of children with rickets to develop respiratory disorders, such as bronchitis and pneumonia, though in one or two careful studies made in children's institutions, it has been found that pneumonia attacked as many children with well-calcified bones as children with radiological evidence of rickets. It is very widely believed, however, and it is probably true, that children with active rickets succumb more readily to pneumonia, partly no doubt, on account of the mechanical obstruction to respiration provided by the deformed and yielding chest wall. Clinical trials of the effect of irradiated milk and ergosterol and of irradiating the skin have yielded conflicting results in studies concerned with resistance to the common cold and with the healing of tuberculous lesions.

There is some evidence that deficiency of the vitamin-B complex may be related to increased susceptibility to certain kinds of infection. Among the recorded observations bearing on this point are those of Bray, who found severe infections common among infants whose mothers were getting an insufficient supply of vitamin B complex. When measures were taken to guard against this deficiency the frequency and severity of infections among the infants fell dramatically.

Vitamin C has been shown to play an important part in determining the resistance of guinea-pigs to tuberculosis, but the evidence regarding its effect in human tuberculosis is indecisive. Observations have been made on the state of saturation with vitamin C of human beings suffering from a great variety of acute and chronic infections. In some of these observations the storage of vitamin C has been found to be reduced, whereas in other observations normal storage is the rule. The special case of rheumatic fever may perhaps be mentioned. It was suggested a few years ago, on the basis of experiments with guinea-pigs, that rheumatic lesions might be caused by a combination of vitamin-C deficiency and a specific infection. This view has not so far been substantiated by observations on children, though it does appear that there is some disturbance in the storage or metabolism of this vitamin in children who show signs of the active rheumatic process.

The only specific mineral deficiency I shall mention in relation to diminished resistance to infection is that of iron. Dr. Helen Mackay found, in her study of nutritional anaemia in infancy, that the incidence of infections of the respiratory tract was almost twice as high among infants who had not been protected from this anaemia by some additional source of iron.

The general impression which one obtains from the kind of evidence outlined here—and I hope that the selection of observations may be regarded as a fair one—is that it is exceedingly difficult to prove definitely the relation of any particular food factor to resistance to infections in man. One is left with the feeling that in so far

as the state of nutrition is connected with resistance to infection, the connexion is rather that good nutrition may determine the course an infection will take than that it will decide whether infection will occur. The evidence available at present in the case of man does not seem to warrant the view that one isolated food constituent is responsible in any specific way for maintaining the resistance of the body to infection in any general sense. On the other hand, there is suggestive evidence that gross malnutrition in a broad sense of the term, or individual states of specific food deficiency, may lower the resistance to established infections. The possibility will have to be considered that an optimum state of nutrition, lasting for a longer time in the life of the individual than has been aimed at in most of the tests so far reported, may be necessary to secure the maximum degree of resistance to infections.

Dr. Harriette Chick: Although famine and pestilence have always been associated with one another in history and there is a widespread conviction that defective nutrition increases susceptibility and lowers resistance to infection, absolute proof of this has been difficult to obtain. The reason for this failure is chiefly that observations on the human subject are complicated by so many variables that it is only by a lucky chance that the effect of one factor only can be studied. Thus, in considering the spread of infectious disease in a community, in addition to (1) the nutritive state of the individual, depending on the dietary, other factors, (2) such as chill, anxiety, and bodily or mental fatigue, will affect the susceptibility of the individual. The chance that infection will take place will also depend on (3) the dose, and (4) the virulence, of the infective agent.

In an epidemic of acute infectious disease, factor (1) will be relatively unimportant in comparison with factors (2), (3), and (4). With a slow and more chronic type of infection, the longer time taken for the inception of the disease renders factors (2), (3), and (4) of relatively less importance. In studying the more chronic infective diseases, therefore, one might expect to trace the effect of nutrition more successfully, and this in fact has been the case.

For example, in epidemics of influenza the richer and poorer classes are alike affected. A disease like measles will sweep through a school of boys from prosperous families as well as through a school run on cheaper lines for poorer children.

With more chronic infections the experience is different. The chronic infective conjunctivitis which was rarely observed among well-situated children was formerly a common occurrence among children in residential Poor Law Schools, but now, under better conditions of diet and management, is rarely seen in these institutions.

The best example perhaps is tuberculosis, the incidence of which is known to be greatly increased by poverty and poor diet. A striking example was afforded by Austria during and immediately after the Great War. In Vienna, where the food deprivation, both quantitative and qualitative, was very severe, the death-rate from tuberculosis was doubled in the period from 1915-1918/19. In the province of Salzburg, on the other hand, where during the same period such important foods as milk, butter, meat, and vegetables were relatively abundant, the tuberculosis death-rate showed little change. It seems probable that infection with tuberculosis is common among all classes but, because of their greater resistance, is more successfully fought by well-nourished people.

TABLE I.—MORTALITY FROM TUBERCULOSIS IN AUSTRIA (ALL AGES).

Year	Vienna City		Salzburg Province	
	No. of deaths	Per 1,000	No. of deaths	Per 1,000
1913	5,937	3.0	527	2.4
1915	6,873	3.4	539	2.5
1917	8,548	4.2	549	2.5
1918	11,531	—	588	2.7
1919	11,490	—	670	—

The above conclusions are well summed up by Clausen at the end of his critical review of the subject (*Physiological Reviews*, 1934, 14, 244): "Susceptibility to infection is not, as a rule, affected by diet; resistance to infection, on the other hand, may be greatly reduced by deficient diet."

In experimental nutrition work with animals, it is possible to arrange for all variables except one, the diet, to be eliminated. Vitamin A has been considered to possess special anti-infective properties. In severe deprivation of this factor, the mucous membrane undergoes such severe structural degeneration that the entrance of infective organisms is facilitated, and after long periods of such deficiency experimental animals invariably show an infective condition of some part of the respiratory system. The work of Dr. Harris suggests that vitamin-C deficiency may also be associated with many infective conditions.

The truth would seem to be that deficiency of any essential dietary factor may predispose to infection by lowering resistance. Mackay, studying anaemia in infants, found that the incidence of infective disease in those medicated with iron was about one-half as great as in untreated control infants.

An interesting demonstration of the influence of the nutritional state upon resistance to infection has occurred in the course of some experiments with pigs, carried out at Cambridge in the Department of Animal Pathology, in collaboration with Sir Charles Martin and Dr. T. A. Birch, who have kindly given permission for publication of the results. The experiments formed part of an investigation of the nutritive value of maize, the aim being to throw light upon the aetiology of human pellagra.

Young pigs, weanlings, and litter mates 30-40 lb. in weight, received one of the following three diets:—

	Group I	Group II	Group III
Maize meal	83	—	76
Wheat	—	20	—
Barley	—	63	—
Pea meal	11	11	10
Casein	4.4	5.3	2.2
Cod-liver oil	3	3	3
Salts	2.5	2.5	2.5
Yeast	—	—	8

After three weeks on the unsupplemented diet the pigs in Group I began to fail in growth, became anæmic, developed diarrhoea sometimes accompanied by vomiting, and rapid loss of weight; they died unless the diet was changed. On post-mortem examination these animals showed a condition of necrotic enteritis with an inflamed and ulcerated colon. All attempts to isolate pathogenic organisms of the *Salmonella* group from blood and stools were unsuccessful.

The pigs in Group II, receiving barley wheat in place of maize, also developed diarrhoea at the same time as those in Group I, but they recovered and growth was resumed. The pigs in Group III, receiving yeast in addition to the maize diet, showed no sign of illness and developed normally and remained in perfect health. The sick pigs in Group I showed a dramatic recovery when yeast was added to their diet.

In this instance one might suppose that the whole series of pigs had a latent infection which could only develop on an unfavourable diet, or that some harmless organism inhabiting the alimentary tract acquired powers of invading the tissues, in other words became virulent, under conditions of malnutrition of the host.

Dr. Leslie Harris referred to some experimental observations made by his colleagues and himself on the relation of vitamin C to infection. A year or two ago some measurements were being made on the excretion of vitamin C in the urine as influenced by the amount in the diet. Some of the experimental subjects happened to develop sharp colds or an attack of influenza and the amount of vitamin C excreted in the urine showed a sudden and marked drop.

This led to extended observations on the effect of different infectious diseases on the excretion of vitamin C. The "usage" of vitamin C seemed to be influenced by infection; in other words, there was an apparent extra need for vitamin C in infections.

Dr. Harris reminded his hearers how, in control subjects *without infection*, the excretion of vitamin C varied according to the amount which had been present in the diet. The more the vitamin C in the past diet, the more was excreted daily in the urine and the greater the state of "saturation". The degree of "saturation" was measured by the amount of vitamin C which overflowed into the urine after a series of large daily test doses had been given. An "unsaturated" subject retained more of the vitamin in his depleted tissues and in consequence less of it appeared in the urine. Intermediate degrees of saturation showed intermediate responses.

Among the "infective" conditions examined were the following: Acute rheumatism, surgical and pulmonary tuberculosis, osteomyelitis, rheumatoid arthritis. Some account had already been published of the results with acute rheumatism and surgical tuberculosis, but the remainder were still in the press.

It would be recalled that Rinehart in the United States had produced in guinea-pigs, by means of a diet deficient in vitamin C plus a superimposed infection, an experimental condition bearing some resemblance to acute rheumatism in man. Rinehart supposed that rheumatic fever in man might have its origin in a state of vitamin-C deficiency combined with infection. Their own observations (Abbasy, Gray Hill, and Harris) related more to the *effects* of rheumatic infection than to its origin. Both in juvenile rheumatism and in surgical tuberculosis in children their results showed that there was a greatly diminished excretion of vitamin C. The response to test doses confirmed the conclusions to be drawn, that in these conditions the body tissues were "unsaturated", and much more vitamin C was used up than normally. (In all these surveys dietary conditions had been standardized by the provision of an adequate fixed amount of vitamin C in the diet for some weeks before the test; and non-infected control subjects on the same diets were always examined simultaneously for comparison.) The same conclusion was reached by further tests when the effect of a constant increased intake of vitamin C in the diet was examined: more vitamin C was used up in the body by the infected children and less was excreted in the urine. (As would appear presently, they had also been able to establish the fact that in infection less vitamin C was present in the body-tissues of experimental animals. This was confirmed by actual analysis, post mortem, of the tissues of infected guinea-pigs.)

A special feature of juvenile rheumatism was that even when the child had become convalescent, and showed no symptoms, and clinically appeared normal, the excretion of vitamin C still remained low and the child could be shown to be relatively unsaturated. This appeared to indicate a condition of latent infection in the convalescent rheumatic. It was evident that the urine test might have diagnostic uses in this direction therefore. This conception of the presence of a latent infective state accorded with clinical experience that a child who had had acute rheumatism was liable to suffer a relapse.

The conclusion to be drawn from these tests seemed to be that, as extra vitamin C was used up in the body, so additional provision of it should be made in the diet. He understood from Dr. Gray Hill that the exhibition of vitamin C in massive doses, in the attempted curative treatment of juvenile rheumatism, had not been found effective. On the other hand, he believed that preventive treatment might offer greater hopes. He suggested that a trial should be made of the prophylactic use of

vitamin C after scarlet fever and streptococcal pharyngitis with the aim of lessening the incidence of subsequent rheumatic complications. In a number of public institutions, for example, it seemed to him that sufficient was known about the average rate of incidence of such complications, and there were sufficient numbers of cases available to make such an investigation probably worth while.

Surgical tuberculosis: osteomyelitis.—With Drs. Abbasy and Gray Hill he had examined children with surgical tuberculosis, and here too urinary excretion of vitamin C was diminished and the patients were below standard in their "reserves". In contrast with juvenile rheumatism, however, there was no evidence of a latent infection, for when convalescent patients were examined they were found to be normal in their vitamin C levels. Similar conditions were found for osteomyelitis.

Pulmonary tuberculosis.—Among the various diseases investigated the most extreme effect, with regard to the vitamin-C "deficit", was met with in pulmonary tuberculosis. The state of unsaturation generally found was very great, and even when the diet had been specially supplemented for some time past the excretion of vitamin C and the response to test doses still stayed very low. These tests and the observations on rheumatoid arthritis were carried out in conjunction with Dr. Philip Ellman.

Rheumatoid arthritis.—The deficit in vitamin C was also striking in rheumatoid arthritis, and gave some evidence of the importance of the much-discussed underlying infective process in this disease. It was instructive to find that as the blood sedimentation rate falls to normal, so the urinary excretion of vitamin C tends to be restored to normal.

Animal experiments.—Tests had been made with Dr. Passmore and Dr. Pagel to examine the state of the "reserves", or the amount of vitamin C in the tissues, of experimental animals as influenced by infection. In such varied infections as tuberculosis, pasteurellosis, and mouse typhoid, and after the injection of diphtheria toxin, the amount of vitamin C in the suprarenals had been found to be diminished. These results confirmed the conclusion drawn from the observations on human beings, made by the more indirect method of urine analysis, that a state of diminished "saturation" of the body tissues existed.

The role of vitamin C in infection.—It was generally agreed that a deficiency of vitamin C reduced the resistance of guinea-pigs to infection. In man also it had been stressed by Hess and others that one of the special characteristics of the "pre-scorbutic" or "subscorbutic" state was the increased liability to infection, and Helen Mackay had concluded in her review on diet and infection, that a case had been made out for vitamin C being involved in combating infection. The experiments described here indicated (1) that there was an increased destruction of vitamin C as the result of the infective process, and (2) that the tissue stores of vitamin C (as in the suprarenal) were diminished in experimental animals in infections. Other workers had stated that vitamin C might have an "anti-toxic" action, for example on diphtheria toxin, both *in vitro* and *in vivo*.

When one came to consider the mechanism by which vitamin C exerted its action one could do little more than speculate, but it might well prove to be of significance that vitamin C was found to be essential for the proper activity of formative cells and for the production of new tissue. In the absence of the vitamin, scar tissue failed to form, and (as he had recently noted) even the hair ceased to grow. Without adequate vitamin C there was degeneration of odontoblasts, ameloblasts, osteoblasts, etc. (Fish and Harris). It might reasonably be supposed, therefore that vitamin C was needed for the formation of blood-cells, and perhaps of antibodies. It should be remembered in this connexion that there was a remarkably high concentration of vitamin C in the leucocytes, and perhaps this might furnish one reason for its increased need in infections. Several workers had pointed out that administration of vitamin C was able to bring about a reticulocyte response.

Finally, Dr. Harris said that he thought the evidence was still inconclusive as to

whether vitamin C in massive doses would help an adequately nourished subject once an acute infection had got a hold. Although claims had been made recently for vitamin C therapy in pneumonia, herpes, and some other conditions, the prospect in prophylaxis seemed more hopeful.

Dr. J. T. Edwards: *A summary of work done on this relationship while working under the Foot-and-Mouth Disease Research Committee, at the Lister Institute and the Pirbright Experimental Station.* A full report of most of the findings has been published in the Fifth Progress Report of the Committee. A review of the statements made by previous workers that size, age, nutrition, and race have a marked influence on the lesions in experimental animals is given in that Report.

White rats.—Systematic investigation was begun early in 1932, following the observation of irregularities in the appearance of lesions in white rats inoculated into the skin of the feet with foot-and-mouth disease virus. Individual animals varied greatly in their susceptibility and it was noted particularly that it was difficult to infect rats which had been kept some time in the laboratory. These rats were fed on a diet of bread and milk, on which they seemed to remain in good health though they did not usually gain in weight. In a preliminary experiment, to see whether more severe lesions could be produced in better-fed rats, Wistar rats were divided into two groups, namely, (i) a well-fed group, fed on a theoretically complete paste diet (Diet N, Korenschevsky, 1922), and (ii) an under-fed group, fed on the bread and milk. Fourteen days later they were all inoculated with virus into the skin of the hind feet. All rats in the well-fed group showed fairly uniform lesions, well-marked local lesions appearing in forty-eight hours, and generalization in three days. The results in the under-fed rats were irregular, varying from no visible lesions, or slight local lesions only, to moderate local lesions and generalization; the lesions were slower in development than in the well-fed group. It appeared that the better-nourished the rats, the more severe the lesions.

A confirmatory experiment was then carried out, placing in the under-fed and well-fed groups, respectively, litter mates from rats specially bred for nutrition experiments. Freshly weaned rats from different litters were placed in the two groups, the sexes being kept separate. At the time of inoculation, seventy days after weaning, the males in the well-fed group had gained on an average 65 grm. more than those in the under-fed group; the females, however, showed a much smaller average difference, namely 23 grm. According to Hutchison and Mottram (1936), the basal metabolism of the adult human female is 83 per cent. that of the adult male, and therefore the bread-and-milk diet may have more nearly satisfied the metabolic needs of the females than those of the male rats. The results of inoculation of virus were very different in the two groups. The greatest difference in severity of lesions was between the under-fed and well-fed males. Those in the under-fed group showed hardly any trace of lesions, whereas, in the well-fed group, all showed severe local lesions and severe generalization. In most of the litters the difference between the corresponding groups of females was not so striking, though still quite well marked. Those from the same litter, when kept under the same conditions, showed lesions almost identical in extent and distribution. Those belonging to different litters reacted differently; this would indicate a familial or hereditary difference in susceptibility.

Susceptibility to infection therefore seems to be influenced by the following factors:—

(1) Diet: That susceptibility is influenced by the nature of the diet, irrespective of its growth-promoting qualities, was suggested by the results obtained in the females of some litters, e.g. in one litter the average weight difference was 22 grm. between the two groups, but the lesions in the two groups were almost the same; in another litter the average weight difference was less, namely 20 grm., but there was a pronounced difference in the lesions. Experimental animals, especially hedgehogs

placed on a good diet, may display great physical activity and fail to gain in weight in the same way as more lethargic individuals. These active animals show a high susceptibility to foot-and-mouth disease infection.

(2) Age.

(3) Heredity.

(4) Sex: The difference in the metabolic needs of the sexes may account largely for the differences in susceptibility between males and females. The observed greater rapacity of males and the greater fastidiousness of females may also influence nutrition, so that the males would be more likely to eat plentifully the paste diet fed to the well-fed groups.

Another experiment confirmed these results. Freshly weaned rats, before inoculation with virus, were specially fed for a short period, namely, eighteen days, upon the "complete" rat diet of basal and supplementary portions described by Korenschevsky, Dennison, and Kohn-Speyer (1932). Two control groups of litter mates were fed respectively on the basal portion only, and on the bread and milk only. A test upon very young rats after this short period of special feeding was considered to be a very severe one for differences in susceptibility. The results showed clearly that the rats fed on the complete diet were the most susceptible; there was hardly any trace of lesions in those fed on the basal portion only. The factor, or factors, promoting increased susceptibility therefore appear to be present in the supplementary portion of the diet.

Rate of onset of increased susceptibility in response to good feeding.—When placed on a good diet (Diet N), after a period of under-feeding, white rats responded very quickly—the males in five days—by showing increased susceptibility to infection. The response was slower in females.

Rate of onset of decreased susceptibility in response to under-feeding.—After several weeks on a good diet, white rats changed to a poor diet (bread and milk) were found to retain their high susceptibility for a long time. After three months the differences observed between litter mates (*a*) changed to the poor diet and (*b*) kept on the good diet were very slight, but after five months there was a clear difference in susceptibility, more striking in the female litter mates. The males therefore seem to retain their high susceptibility, after change to the poor diet, longer than the females.

No difference was found between wild rats and tame (white) rats when both had been kept for some time on a good diet before being tested for susceptibility.

Whether any component of the diet was particularly concerned with causing increased susceptibility to foot-and-mouth disease infection had not been determined. Rats with very severe symptoms of vitamin "A" deficiency did not become completely insusceptible to infection. The addition of raw liver and carrot to the bread-and-milk diet produced a distinct and rapid increase in susceptibility, which acted in a few days. The decreased susceptibility of rats placed on an inadequate diet was found to be associated with the constant symptom of anæmia. It is possible that the addition of raw liver to the bread-and-milk diet prevented the occurrence of anæmia and it may have also been an important factor in producing increased susceptibility to foot-and-mouth disease. The impression gained from observations upon the smaller experimental animals has been, however, that susceptibility to infection is influenced, not so much by any specific ingredient in the diet, but by the degree to which nourishment promotes metabolism generally in the animal body.

Guinea-pigs.—It is a common observation that guinea-pigs, which have been inoculated in large numbers in foot-and-mouth disease research laboratories for diagnostic and other tests, present considerable differences in susceptibility, small guinea-pigs and those in a poor state of health being much less likely to develop lesions. Guinea-pigs are, however, much less satisfactory than white rats for determining the effects of variation in nutrition upon susceptibility to infection. They are naturally herbivorous and refuse food and starve when there is any considerable

departure from their ordinary diet; the effects therefore tend to become those of simple starvation. With sudden change in feeding, or bad feeding, however, they become resistant. For example, on one occasion at Pirbright, the supply of cabbage and carrots ran out, and the stocks of guinea-pigs were fed on green weeds, mostly dandelion leaves and roots; these caused diarrhoea and a high death-rate. The animals showing these symptoms were resistant to inoculation.

Hedgehogs.—Whereas guinea-pigs and rats can be infected with the foot-and-mouth disease virus by inoculation only, hedgehogs can be readily infected with this virus by contact with diseased hedgehogs also, and the disease is more severe and fatal than in any other species known to be susceptible. Stocks for research are captured wild, and so it is difficult to carry out any satisfactory experiments to find out the effects of nutrition upon susceptibility to infection. Bodily condition is, however, a most important factor in determining susceptibility, and this factor renders foot-and-mouth-disease research in these animals particularly difficult. Severity of the disease in inoculated animals has been found to correspond closely with bodily condition. The better the condition the more severe the disease.

When first brought into captivity, hedgehogs, particularly the larger, and presumably older, ones, often refuse food for long periods, which may extend to nearly two months, lose weight rapidly, and many die from starvation. While they are losing weight, they always show a high resistance to infection, and artificially set-up outbreaks die out rapidly when such animals are used for transmission of the disease. On arrival, each hedgehog is caged separately, because they are likely to attack each other and cause fatal sores when they are first brought in and are in falling condition. The following diet has been found from experience to be most suitable and maintains them in the good bodily condition necessary for ensuring uniformly high susceptibility to infection with the virus of foot-and-mouth disease.

ROUTINE HEDGEHOG DIET

Minced meat	11 lb.
Suet	2½ "
Liver	3 "
Root vegetables	{ potatoes	8 "
	{ carrots or swedes	8 "
Wholemeal biscuit	8 "
Skimmed milk powder	1½ "
Frozen egg	1 "
Salt mixture	2 oz.

Steam together until cooked (a) suet and minced meat, and (b) chopped potatoes and roots. Pass potatoes and roots through mincer. Mix milk powder with 2 quarts of water, add to wholemeal biscuit; steam together until soft. Dust salt mixture into mixed food. Add minced raw liver and frozen egg. Mix together all food ingredients thoroughly. Feed once daily *ad lib.* in the evening; fresh water daily *ad lib.*

When hedgehogs hibernate their metabolism is greatly lowered and they become completely resistant to infection. If, however, the virus has already begun to multiply in them when they enter this state, it remains dormant in their tissues for as long as two months and probably longer. When they become active again, the virus multiplies and sets up the clinical disease, and this has been found to be transmissible to healthy hedgehogs by contact. To obtain regular severe infection in hedgehogs experimentally it is therefore necessary to use only such as are feeding well and showing a normal, warm-blooded, temperature, that is, those in which metabolism is most active.

Concurrent bacterial infection.—A preceding or intercurrent bacterial infection renders all these small animals highly resistant to foot-and-mouth disease infection. This resistance is probably caused by the state of under-nourishment produced. In hedgehogs, on the other hand, infection with the virus of foot-and-mouth disease,

especially a severe infection contracted naturally by contact, causes, as in several other virus diseases of animals, serious secondary multiplication of bacterial invaders, e.g. *Salmonella enteritidis* (Gaertner) in the alimentary tract, and *Brucella bronchiseptica*, pasteurella and streptococci in the respiratory tract.

Age.—The fact that the small animals dealt with in this paper can be infected with the smallest dose of virus and show the most severe lesions when they are presumably fittest, namely, when they have nearly finished, but not completed, their stage of growth, suggests that the animal body becomes more and more susceptible to infection with the virus of foot-and-mouth disease when healthy metabolism or physical fitness is increased. Very young and old animals are relatively resistant.

Cattle and other large animals.—Experimental work to determine the relation between the state of nutrition and susceptibility to foot-and-mouth disease infection has not yet been carried out upon the larger, naturally susceptible, animals. It has often been noticed, however, that when cattle and other larger animals are in low condition they do not react well to inoculation with the virus. The records of field observations in temperate countries give little information upon the relationship, although it is often observed in outbreaks that high-class stock, fed and kept in the best conditions, suffer more severely than lean beasts when the disease is allowed to run its course. According to Hutyra and Marek (1920), foot-and-mouth disease spreads on the Continent of Europe with particular rapidity during the warmer period of the year, while in the winter it does not occur so extensively. They attribute this increased prevalence in warm weather to the greater traffic in cattle.

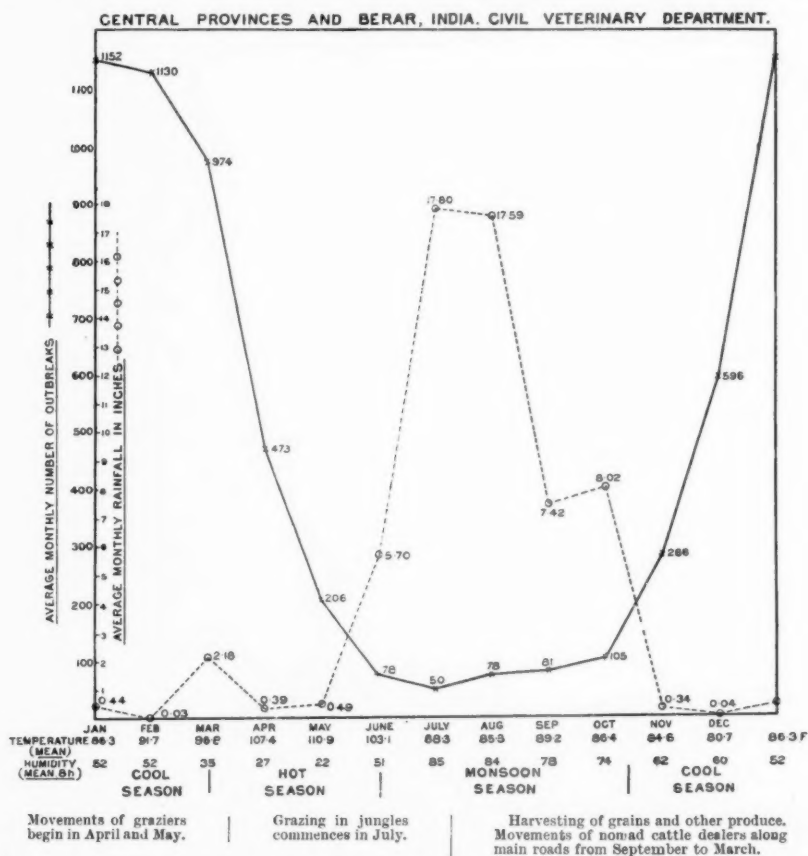
In hot climates, where there is little or no fodder storage and where there are great seasonal fluctuations in the natural food resources dependent upon the annual monsoon, with consequent cyclical fluctuations in the bodily condition of the cattle, one expects to find the most striking evidence of the relationship between foot-and-mouth disease susceptibility and the state of nutrition of the animals. Bevan (1932, 1933) described a very mild form of foot-and-mouth disease which occurred in Southern Rhodesia in 1931, which spread slowly and could only be transmitted with difficulty. This form occurred in the dry season, but became more active and severe after the rains. It seems probable that its mild character was in part determined by the scarcity of fodder and that the more severe phase of the epizootic reappeared when the pasture had improved.

Records showing the prevalence of foot-and mouth disease and its epizootic course in India at different seasons are shown in the chart (p. 48). This gives a composite curve showing the average monthly returns of outbreaks of foot-and-mouth disease in the Central Provinces and Berar, India, for the six years 1926-31 inclusive, in relation to a curve showing the average rainfall during the same period; other meteorological data are given below (compiled from data collected by the late Director of the Civil Veterinary Department, the late Major R. F. Stirling). It was thought that the records of disease incidence in this province, which is just south of the Tropic of Capricorn, would be particularly valuable, because there is very little variation in climatic conditions from year to year, and every year there is a very striking alternation of "hot weather" and "cold weather" conditions. It will be seen that foot-and-mouth disease becomes very prevalent, as it does elsewhere generally in India, during the "cold weather" season of the year, when the cattle are in their best condition, owing to climatic and pastoral conditions. Afterwards, with the coming of the "hot weather" season, from March to the middle of June, through tropical heat and lack of rain, the fodder resources disappear to such a degree that a very large proportion of the cattle experience great shortage and many die from starvation. At the same time, foot-and-mouth disease disappears to such an extent that rare mild outbreaks only are reported.

The records of other countries which experience annually regular profound climatic variations need to be examined in order to ascertain whether these related

phenomena of seasonal periodicity in foot-and-mouth disease and the nutritional state of the cattle can be correlated.

Conclusions.—The conclusions to be drawn from the evidence presented are opposed to much current opinion regarding infectious diseases in general. The view commonly held, and apparently more widely applicable, is that low physical condition, such as that found in the under-nourished, the very young, the old and



Composite chart showing curves of the average monthly number of outbreaks of foot-and-mouth disease during the six years 1926-1931, inclusive, and of the average monthly rainfall during the same period. The monthly returns for the average mean temperature and relative humidity (8 h.) are also given below the chart.

sickly, makes them an easy prey to any current infection. The facts presented in this contribution can be paralleled, however, to some extent by experience with other diseases in veterinary medicine and pathology. It is generally accepted that strong, well-grown young cattle are more susceptible to blackleg and anthrax than lean cattle, and perhaps in some infections of sheep, such as braxy, there is a similar tendency.

The experiments upon small animals described in this paper confirm the observations of others that foot-and-mouth-disease infection is most severe in well-grown and well-nourished animals. In fact, they are most susceptible when they are in prime condition and at the prime of life.

REFERENCES

- BEVAN, L. E. (1932), *Tr. Roy. Soc. Trop. Med. and Hyg.*, **26**, 89; *ibid.* (1933), **27**, 105.
HUTCHISON, R., and MOTTRAM, V. H. (1936), "Food and the principles of dietetics", 8th ed. London, p. 71.
HUTYRA, F., and MAREK, J. (1920), "Special pathology of the domestic animals", *Trans. Mohler and Eichorn*, **1**, 360.
KORENCHEVSKY, V. (1922), *Med. Res. Council Spec. Rep. Ser.*, No. 71, p. 7.
KORENCHEVSKY, V., DENNISON, M., and KOHN-SPEYER, A. (1933), *Biochem. J.*, **27**, 557.

Dr. H. Warren Crowe said that some experiments which he conducted a few years ago might be of interest, and perhaps throw light on this question of nutrition in relation to infection. In experiments in the production of arthritis in rabbits by injections of arthrotropic streptococci, the appearance of arthritis in all rabbits injected became quite regular as the technique became standardized. Professor H. A. Harris suggested that the effects might be more obvious and rapid if the rabbits had been previously fed on a non-vitamin dietary. For this experiment thirty-six rabbits were fed exclusively on a certain cereal prepared for consumption by cooking in super-heated steam, so that all vitamin content was destroyed. After a month or six weeks these rabbits had lost weight, the fur was roughened, and they appeared fairly sick. The rabbits fed in this way were then injected three at a time, three healthy rabbits in each case being used as controls. The latter developed arthritis in the expected manner, but the non-vitamin rabbits, broadly speaking, developed no arthritis at all. The reason for that should be clear when one realized that rheumatism and arthritis were diseases of tissue reaction. If the tissues did not react, there would be no arthritis. If, as the result of malnutrition, the tissues failed to react, then arthritis would not develop.

Possibly, then, the experiments quoted by Dr. Edwards in regard to foot-and-mouth disease had the same explanation. If the symptoms of this disease were due to tissue reaction, under-nourished animals would not be so likely to show lesions.

With regard to the epidemic of influenza of 1918 referred to by previous speakers: The same explanation would account for the fact that it was the young, strong, healthy soldiers who died so rapidly and in such large numbers, rather than the under-nourished civil population. He (Dr. Warren Crowe) had had to perform several post-mortem examinations, and the cause of death in every case had been mechanical; owing to the intense reaction the patients had been drowned in their own secretions.

Mr. A. L. Bacharach called attention to the fact that the total effect of several food constituents affecting resistance to infection was integral rather than a sum. The effect of one addition, or subtraction, might well be masked by the limiting effect of shortage of another substance. This principle, it seemed to him, was not always borne in mind in interpreting results of investigations falling into Professor Cowell's third category, in which it had been attempted to examine the effect of specific dietary conditions on infections in a group of human subjects. Ascorbic acid (vitamin C) appeared to be utilized at above the normal rate, as evidenced by a condition of sub-saturation, not only in the febrile conditions described by Dr. Harris, but also in benzene poisoning, as well as during lactation and pregnancy. The amount secreted in the milk was, apparently, not sufficient to account for the extra utilization. Any physiological or biochemical explanation of the role of ascorbic acid in fevers must take into account these other observations if, as he believed they would be, they were confirmed and generally accepted.

Dr. Curjel Wilson referred to the nutritional research aided by the Royal Society which was being carried out in India. Six thousand nutritional examinations (on the lines of those recently carried out in Britain under Sir John Orr and Dr. Magee), were made on children between the ages of 5 and 15 years, among wheat-eating races—Hindu, Muslim, and Sikh—in Northern India.

In addition, in view of Dr. Aykroyd's recent publications (*Indian J. M. Research*, January 1937) on the frequent occurrence of signs of deficiency disease in Southern India, the signs of deficiency disease were sought for among these northern children and a diet survey carried out on 120 families among these races living both under urban and under rural conditions. The results of the research were in course of publication.

With regard to malaria: Over 2,000 children were examined in areas recognized by the Malarial Survey of India to be highly infected. The signs of diet deficiency, phrynoderma, angular and buccal stomatitis, and eye conditions were practically absent. He understood that similar observations had been made by Dr. Nicholl on malaria in Ceylon.

Section of Dermatology

President—H. W. BARBER, M.B., F.R.C.P.

[May 20, 1937]

Molluscum Sebaceum.—HENRY MACCORMAC, C.B.E., M.D.

This patient has been brought to illustrate molluscum sebaceum, a condition which Dr. Scarff and I have recently described, and one that has caused some controversy and difference of opinion. She is a woman aged 68 who first attended in 1931 on account of psoriasis. As far as I know she has never taken arsenic. The condition is of recent development, growing from normal skin, reaching its maximum development in four weeks, and then remaining stationary. It consists of a pea-sized hemispherical solid lesion capped with an apical adherent scale. Its situation on the middle area of the face—to the left of the nose, in this case, is characteristic.

Dr. Savatard and Dr. Adamson both regard this type of lesion as belonging to the malignant group, a button epithelioma. For obvious reasons I have refrained from interfering with the tumour, and there is therefore no microscopic evidence in this patient. The microscopical section from the case previously described in the *British Journal of Dermatology*, 1936, 48, 624, has been shown to-day, and neither Professor J. McIntosh, Dr. R. Scarff, nor I regard the appearances as those of a malignant growth. I have further watched the behaviour of these lesions in other cases and in none has the subsequent course followed that of a malignant growth, which, taking into consideration its initial rapid development, should show a high grade of malignancy.

Discussion.—Dr. W. N. GOLDSMITH said he was much interested in these cases described by Dr. MacCormac, all of which were in old people. A short time ago, however, he had had at St. John's, a little boy who had a lesion on the cheek which seemed clinically unusual. It looked most like an epithelioma, but with a peculiar central dimple filled with a horny plug.

The appearance was very like that of the tumour shown to-day. It had been there for six weeks, having first appeared soon after a slight scratch. There had been nothing at the site, such as a mole, previously. At first it had been taken for a septic spot and fomented, but it did not disappear; when first seen by the speaker it was considered a granuloma or some kind of epithelioma. It was excised and showed a deeply invaginated depression, which corresponded with the central horny plugging. Dr. Muende thought the histology was that of prickle-celled epithelioma. Dr. Freudenthal thought it bore resemblances to Dr. MacCormac's cases and Dr. MacCormac agreed. It therefore seemed that this kind of lesion could occur in quite young people after injury. He did not think its exact nature had yet been determined.

Dr. H. SEMON congratulated Dr. MacCormac on bringing these cases forward and drawing attention to their peculiar histopathology, which had not so far been sufficiently studied.

He deprecated the use of the term "molluscum", however, as very likely to give rise to a confusion with the other disease—molluscum contagiosum, with which they were all familiar.

Dr. S. E. DORE said that frequently in textbooks on pathology there was no mention of sebaceous tumours other than sebaceous cysts, and adenoma sebaceum. Did Dr. MacCormac consider this case an example of a single sebaceous adenoma?

Dr. FREUDENTHAL said he hoped Dr. MacCormac would produce further evidence in favour of his molluscum sebaceum theory to permit the question to be discussed more fully.

The term molluscum sebaceum should, if possible, be replaced by another, as Hebra and Kaposi used it as a synonym for molluscum contagiosum.

Dr. MACCORMAC (in reply) said he thought that Dr. Goldsmith's and Dr. Freudenthal's patient was an example of "molluscum sebaceum", although he had not previously met with the condition in one so young. The name was admittedly a bad one: it was chosen because of the resemblance in the microscopic structure to molluscum contagiosum; the papilloma was possibly due to a virus infection as in the common wart. He did not consider that there was any relationship between "molluscum sebaceum" and sebaceous adenoma.

Granulosis Rubra Nasi.—A. D. K. PETERS, B.M.

The patient is a delicate-looking boy aged $9\frac{1}{2}$ years; high-grade mental defective, of illegitimate birth. The parents, half-brothers, and half-sisters are unaffected and are not suffering from any constitutional diseases.

The condition was first noticed at the age of 2 years, after the child had grazed his nose.

On examination.—Beads of perspiration are present over the lower part of the forehead, eyebrows, nose, upper lip, and chin. They re-occur immediately after they are wiped away. There is a diffuse red area on the bridge and tip of the nose; the column and edge of the nostrils are left clear. The colour gradually fades away into that of normal skin. It is due to vascular dilatation, being lost on diascopy. The nose feels cold to the touch.

Numerous small telangiectases are present on the nose, cheeks, and chin. Round dark red papules, the size of a pinhead are scattered over the bridge and tip of the nose. The red colour and perspiration are increased by emotion and in hot weather. Patient's general health is fairly good although he has frequent colds. There is no history of vasomotor rhinitis. The boy does not feel the cold and does not suffer from chilblains, or hyperidrotic hands and feet. He has no indigestion.

On general examination he was found to have a rhinitis, a protuberant abdomen, and an undescended right testicle which may be felt in the groin. The palms of the hands are normal, but feel cold to the touch.

He has been treated with lotio calaminae cum plumbi, m x of hydrochloric acid before meals, and a nasal oil. There has been slight improvement.

Tuberculoid Leprosy.—F. JACOBSON, M.D.

The patient, an Indian student, aged 25, some years ago in India had a lesion on the back of the left hand, which was for some time associated with numbness and tingling. It healed up after taking some Indian medicine, and now after seven months in this country there is a lesion on the back of the right hand (fig. 1). This lesion appeared soon after signs and symptoms which are suggestive of a sensory disturbance in the area of the right ulnar nerve (fig. 2). The bacteriological findings are negative, the histological picture is that of a tuberculoid or sarcoid of Boeck.

In spite of the fact that we did not succeed in finding Hansen bacilli, and that the histological picture does not exclude the possibility of an actual tuberculoid or sarcoid lesion, I think it justified to diagnose this as tuberculoid leprosy for the following reasons:—

(a) In the vast majority of all cases of *tuberculoid* leprosy described in the literature Hansen bacilli are exceedingly seldom found.




(b) The clinical and histological picture is the same as that in many cases of tuberculoid leprosy described by authors who had had great experience in the diagnosis of leprosy in countries where this disease is endemic.



FIG. 1.



FIG. 2.

-  Loss of sensation to heat and cold
-  Diminished sensation to pain
-  Diminished tactile sensation

[Drawing kindly supplied by Dr. F. Siegheim.]

(c) The involvement of the ulnar nerve area together with the fact that the patient comes from a country, and belongs to a race, in which leprosy is endemic, and in addition to this has a history which is somewhat suspicious of a previous attack.

The first case of tuberculoid leprosy was described by J. Jadassohn in 1898. Later Klingmüller, Kedrovski, and Unna published similar observations. In 1923 Darier and Pautrier reported four cases. Further knowledge we owe to a number of publications from tropical countries and also from Norway. From this it is evident that cases of tuberculoid leprosy are not so rare as was formerly thought. For instance in Reiss' clinic in China, 40% to 50% of leprosy cases were of the tuberculoid type.

In my opinion it does not greatly matter whether one labels this "tuberculoid" leprosy or "sarcoid" leprosy. Reiss, for instance, states that the lesions in his cases of tuberculoid leprosy resembled Boeck's sarcoid or tuberculosis cutis luposa, or verrucosa. Also Quérangal des Essart and Lefrou who described "Les sarcoïdes de la lèpre" consider the sarcoid type to be only a special tissue reaction to the leprosy. The main point according to their experience is that in the sarcoid type of leprosy one finds Hansen bacilli much more often than in the tuberculoid form. It is well known that it is often impossible to differentiate sarcoid from leprosy histologically. On the other hand, it is as frequently impossible to differentiate between tuberculoid and sarcoid which, as Darier states, have intermediate and transition forms, both clinically and microscopically. Therefore it seems to me unnecessary to complicate the classification of the different forms of leprosy by introducing a new subgroup, namely sarcoid leprosy.

From a prognostic point of view the tuberculoid form of leprosy is the most favourable, and seems to be an attenuated variety.

Therapeutically, I propose to inject hydnocarpus esters locally into, and around the lesion.

BIBLIOGRAPHY

- DARIER, "Les tuberculoides de la lèpre", 31ème Conf. Int. de la Lèpre, Strasbourg, 1923.
 JADASSOHN, J. "Ueber die tuberkuloide Veränderung der Haut bei nicht tuberöser Lepra", *Verhandl. d. deutsch. dermatolog. Gesellsch.*, VI. Dermatol. Congr., Strasbourg, 1898.
 KLINGMÜLLER (1927), "Ueber tuberkuloide Lepra", *Arch. f. Dermat. u. Syph.*, **153**, 584.
 Id., "Die Lepra", i. Jadassohn's *Handb. d. Haut- u. Geschlechtskr.*
 LEFROU et QUÉRANGAL DES ESSART, "Les problèmes de la lèpre tuberculoïde", *Bull. Soc. path. exot.*, **28**, 301-316.
 LIE, H. P., "Les tuberculoides de la lèpre", 31ème Conf. Int. de la Lèpre, Strasbourg, 1923.
 PAUTRIER and BOEZ, "Cas de lèpre tuberculoïde", 31ème Conf. Int. de la Lèpre, Strasbourg, 1923.
 QUÉRANGAL DES ESSART et LEFROU (1935), "Les sarcoïdes de la lèpre", *Bull. Soc. path. exot.*, **28**, 626-639.
 REISS, (1935), "Tuberculoid leprosy amongst Chinese", *Delib. Congr. Derm. Int. IX. -i.*, Budapest, pp. 583-590.
 Id. (1934), "Tuberculoid lepra, a clinical entity or a histo-pathological reaction". From IX. Congr. of the F.E.A.T.M., 699-734. Vol. i. Nanking.
 TISSEUIL (1931), "Contribution à l'étude des tuberculoides de la lèpre", *Bull. Soc. path. exot.*, **24**, 1898-1902.
 WADE, H. W. (1932), *Proc. Roy. Soc. Med.*, **25**, 1023 (Sect. Derm., 47).
 Id. (1934-35), "Tuberculoid changes in leprosy", I, II, III, IV, *Internat. J. of Leprosy*, **2 passim**; **3**, 121.

Lichen Nitidus.—ROBERT KLABER, M.D.

This boy, aged 9, has had successful operations for congenital pyloric stenosis and for a squint. He usually enjoys good health.

Seven months ago.—The eruption was first noticed on his wrists when he was in hospital for the operation on his eyes. Since then, the eruption has been observed to have a wide distribution, though in some areas it is said to appear and disappear within a few hours. The disappearance is said to be helped by exposure to sun and air, but it seems possible that this is only an optical illusion. There is slight irritation only when a new group of lesions is appearing.

The eruption is fairly symmetrical and shows as extensive sheets, especially round the shoulder girdles, elbow flexures, wrists, groins, and back of the neck. Papules are also present, though less evident, on the penis and on the sides of the nose. The lesions consist of innumerable extremely small iridescent flat-topped papules. Most are white or skin-coloured, but in a few areas they are more reddish.

There is no personal or family history of tuberculosis.

Biopsy.—Three small papules in line were excised together. Section shows each papule represented by a globular infiltration, which has caused pronounced flattening of the overlying epithelium. The infiltrate consists chiefly of small round cells with only a few endothelial and giant cells, lying in a loose oedematous reticular stroma. These appearances have been described as characteristic of lichen nitidus.

Postscript (14.6.37).—There is no doubt regarding the disappearance of the lesions after sunbathing. When the boy was seen a week ago, there was well-marked solar pigmentation, and only a few ill-defined lesions were to be seen in unexposed areas.

? Chloasma Virginum Periorale.—ROBERT KLABER, M.D.

This girl, aged 20, has noticed, for two months only, bands of pigmentation surrounding the lips, about 1 in. in diameter.

She states that she never uses any scent of any kind on the face. She does, however, occasionally use lavender-water on her handkerchief, though never eau-de-Cologne.

Menses regular. No marked seborrhœa.

This case resembles one shown by Dr. Corsi two years ago.¹

The distribution does not seem to suggest chloasma uterinum. I do not know whether the pigmentation could have resulted from the use of scent on the handkerchief.

Discussion.—Dr. H. CORSI said that in the case which he had shown in 1935, it was noticeable, as in Dr. Klaber's case, how abruptly pigmentation stopped a few millimetres from the red lip-margin, making it improbable that this pigmentation was the result of using eau-de-Cologne or other scent. The term "chloasma virginum" was not good: all that could be said was that the condition occurred, as a rule, in young women; marriage was no cure for it.

Dr. HUGH GORDON said that a patient of his, who was a fair-complexioned girl, had well-marked upper-lip chloasma, with sharp margins. It was disfiguring in the summer, but practically disappeared in the winter. Since he had had that case it had been suggested that such patients had a deficiency of vitamin C.

Dr. I. MUENDE said that the pigmented area seemed to him to correspond closely to the moustache and beard area.

Benign Lymphogranulomatosis with Ocular Symptoms.—HUGH GORDON, M.C., M.R.C.P.

The patient, a woman aged 34, suffered from psoriasis from the age of 14. In 1931 both eyes were inflamed following a motor journey. They were painful at first, but later the pain subsided. The sight, however, failed progressively from that time in each eye.

She was admitted, under Sir Stewart Duke-Elder, to St. George's Hospital in June 1934, with deep corneal nebulae centrally in each eye and vascularization. Both pupils were bound down by adhesions and occluded by exudate. The general condition was diagnosed as one of deep keratitis associated with iritis, no cause being found.

She had at that time fairly extensive psoriasis. On being referred to the Skin Department it was noticed that, in addition to the psoriasis, she had about five

¹ *Proceedings*, 1935, 28, 1169 (Sect. Derm., 53).

sarcoid lesions on the chest and back. She said that these had first appeared in 1932—i.e. shortly after the eyes first began to give trouble. A biopsy showed the typical picture of benign lymphogranulomatosis.

At that time there was no lymphatic enlargement. A skiagram of the chest showed very extensive fibrosis, suggesting to the radiologist a diagnosis of miliary tuberculosis or alveolar carcinomatosis.

A bilateral iridectomy was performed in 1934 together with the extraction of the lens from the right eye. Exudate, however, closed the iridectomy area and no obvious improvement was obtained. In 1936, a further iridectomy was performed, again without any improvement resulting, since as on the first occasion, the anterior chamber filled with a dense white exudate.

Mr. Geoffrey Bridgeman, who kindly furnished me with the report on the eye condition (by permission of Sir Stewart Duke-Elder) says that the optic condition is one of chronic plastic iridocyclitis, showing relapses whenever any intra-ocular operation is undertaken.

The patient has unfortunately not been seen from the dermatological point of view since 1934. She now presents a very extensive sarcoid eruption covering the chest, back, and arms. This in appearance and distribution strikingly resembles a secondary syphilide. The lesions are circinate in many places, with involuting centres. Some lesions have healed, leaving a faint scarring. On the forearms there are many papules the size of a split pea—some of them tending to be grouped. All the lesions are epidermal. This eruption has been present for eight months and is now fading.

Tonsils slightly enlarged; epitrochlear glands palpable; spleen palpable. A skiagram of the chest shows that the fibrosis is less in extent than it was in 1934. Bones unaffected. Wassermann and Mantoux reactions negative.

On physical examination the chest appears normal. Apart from her eyes her general health appears to be completely unimpaired. The case is of interest since serious ocular manifestations do not appear to be common in the reported cases of benign lymphogranulomatosis. In this case they have been the first symptoms to be noticed and have resulted in practically total blindness.

The skin eruption is unusual, on account of its widespread nature and apparently sudden onset. After having a few chronic nodules of the more usual dermal type which spontaneously disappeared, she suddenly has, as it were, exploded in the manner of a secondary syphilitic eruption.

¶ ? Addison's Disease.—HUGH GORDON, M.C., M.R.C.P.

Patient, a woman aged 60, has noticed an increasing pigmentation of the skin for two years. During the last six months a large number of small brown spots have appeared, chiefly on the axillæ and groins, but also on the trunk. She has lost a stone and a half in weight during the last eighteen months but otherwise feels well. She attributes the onset of the pigmentation to two severe shocks during the same period. After each shock she noticed definite access of pigmentation. There has been no vomiting or gastro-intestinal trouble, and no muscular weakness.

On examination.—The trunk is naturally and evenly pigmented. In the axillæ are a number of plugged follicles. A large number of pigmented warts are present on the abdomen. The soft palate shows definite pigmentation. Blood-pressure is 98/60. On clinical examination there is no evidence of abdominal carcinoma.

The case is shown with the tentative diagnosis of either Addison's disease or acanthosis nigricans. It has features of both disorders but does not appear to be quite typical of either. It is suggested that the pigmentation is the result of some adrenal dyscrasia, possibly precipitated by shock.

Discussion.—Dr. H. SEMON asked whether pigmentation was not a late symptom in Addison's disease. This patient had no vomiting and no evidence of weakness, therefore he thought that Addison's disease could be excluded. The character of the eruption and the dryness of the skin rather suggested arsenic as cause.

A MEMBER asked whether the blood-sodium had been estimated.

Dr. GORDON replied he could not say whether the blood-sodium had been estimated; the patient had not been really under his care. He agreed that the evidence in favour of the condition being Addison's disease was very indefinite. The patient had had thyroid but not arsenic.

Urticaria Pigmentosa.—GODFREY BAMBER, M.D.

Mrs. D. J., aged 32. The history is that the red spots first appeared six years ago on the outer sides of the arms; since then they have gradually extended over other regions. They do not itch. She has taken no drugs which might account for the rash.

Present condition.—The arms and legs are thickly covered with lentil-to-peasized spots which vary in colour from deep red to dark brown. Some of the lesions are slightly raised above the surface of the surrounding skin. Vigorous rubbing failed to produce urticaria in the lesions.

Histological examination shows, in the middle and upper third of the cutis, a slight perivascular infiltration which in some places is mostly formed by mast cells.

Phenolphthalein Eruption.—GODFREY BAMBER, M.D.

Mrs. B., aged 47.

History.—Seven months ago there appeared on the arms several itchy, red, slightly swollen patches which lasted for a few days and then disappeared, leaving brown marks which have persisted. Since the first appearance the patches have occasionally flared up.

Present condition.—On the arms, chiefly the extensor aspect of the forearms, are deeply pigmented round patches up to two inches in diameter.

A diagnosis of a fixed eruption due to phenolphthalein was made. The patient was found to have taken, as an occasional aperient, a proprietary preparation which contains phenolphthalein. She was asked to take another tablet, after which the eruption flared up again.

Dr. ELIZABETH HUNT said she had had a number of patients who showed intolerance to a phenolphthalein-containing preparation, but none showed the eruption so well as in this case. As soon as the preparation was stopped the eruption disappeared.

Diphtheroid Ulceration.—LOUIS FORMAN, M.D.

R. H., male, aged 30.

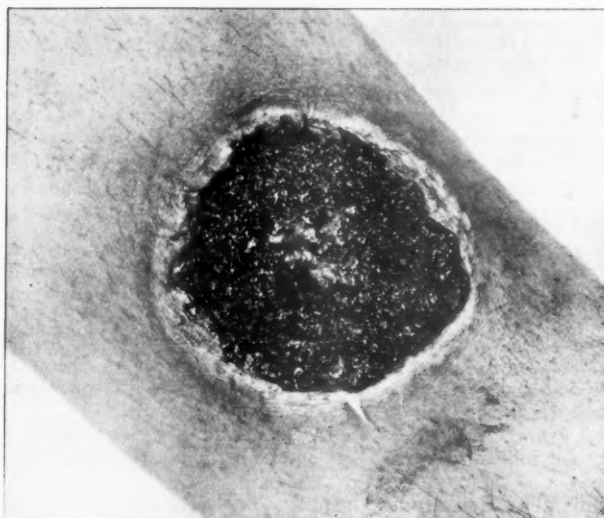
In April last blisters developed on the elbows and ankles; they became hæmorrhagic and discharged pus. There were small hæmorrhagic vesicles on the soles. Seen for the first time in May when there were breaking down granulomata on the elbows and ankles and there was a septic-looking ulcer on the left shin.

In the differential diagnosis a halogen eruption and pyoderma were considered.

11.5.37: The ulcer on the shin had increased in size and become painful. The edge was oedematous and purple, showing the horny layer detached; the floor was covered with an adherent slough which when removed revealed bright red granulations.

13.5.37: Cultures, superficial and deep, gave growths of a moderate-sized diphtheroid showing mild polar staining. Otherwise only staphylococci and a few obvious saprophytes were present (Dr. F. A. Knott).

The ulcer has been treated with liquid permeyase and with the jelly, and is showing signs of healing. One corner is still rather characteristic.



Ulcer showing detached horny layer which represents the remains of superficial pustules, and characteristic dry red granulations.

Discussion.—Dr. H. SEMON said that in such a case as this, in which the diphtheroids had been isolated, it would be of value to try the effect of inoculating some other area. A positive result would more firmly establish the ætiology.

The PRESIDENT said he thought that the ætiology of these cases was beyond dispute. In both of his (the speaker's) own cases, Dr. F. A. Knott had withdrawn sero-purulent fluid with a hypodermic syringe by plunging the needle through the unbroken skin covering the inflamed œdematous edges beyond the margins of the actual ulcers. On staining the fluid thus obtained, the diphtheroid organism was the only one observed and many of these organisms were lying inside the leucocytes.

With regard to the relationship of this organism to other diphtheroids, it was morphologically and in its sugar-reactions closely allied to the Klebs-Löffler bacillus and quite different from Hoffmann's bacillus and the *B. xerosis*.

Shortly after the article by Dr. Knott and himself (*Brit. J. Derm. and Syph.*, 1920, **32**, 71) appeared, Sir E. Graham Little had shown a similar case, but in that case, in addition to the skin, the mucous membrane of the mouth was affected. Dr. John Matthews isolated a diphtheroid bacillus differing only slightly from the *B. diphtherie*.

Injections of anti-diphtheric serum had been given in the first case but apparently without benefit. The serum had, however, protected guinea-pigs against the effects of experimental inoculation.

? Lichen Planus: Case for Diagnosis.—R. T. BRAIN, M.D.

Patricia O. was first seen by me January 27, 1937, at St. John's Hospital for Diseases of the Skin, at the age of 7½ months.

Her mother said that the infant had had eczema on the knees and wrists since birth; a few months later papules appeared about the knees and elbows, and a month ago the skin became rough and an eruption appeared on the face; irritation was slight. Raised spots then occurred on the limbs. The child had not been vaccinated and there was no knowledge of her or of her mother having had bromide or iodide. The mother's blood Wassermann reaction was negative.

On examination.—Rather undersized but fairly well nourished. On the arms and legs were numerous dull red irregular, papules, some verrucose in appearance and others capped by firm yellowish crusts and scales. Some resembled urticarial papules, and the yellowish translucent appearance suggested deep vesication. The lesions were aggregated into clumps and rings and circinate figures producing patterns like erythema multiforme. The condition was first regarded as a toxic eruption and hydrargyrum cum creta gr. $\frac{1}{2}$ was given twice daily and a calamine and phenol lotion was prescribed. No improvement followed; the lesions became firmer and circinate forms more numerous. A biopsy was made on February 3, and a blood-count taken on February 7. Neither throw much light on the diagnosis.

Pathological report (Dr. I. Muende).—There is acanthosis, proliferation of the stratum granulosum, and marked hyperkeratosis affecting the upper third of the hair follicles and sweat ducts. At about the juncture of the upper and middle third of the hair follicles there is an acute folliculitis associated with an accumulation of polymorphonuclears in the follicle wall. In the upper part of the corium there are numerous small foci of vacuolated endothelial cells and giant cells of the foreign body type. The collagen in the pars papillaris is partly fragmented.



Blood-count: Hb. 80%; W.B.C. 16,300 per c.mm.; polys. 40%; lymphos. (small 28%, large 17%) = 45%; large monos. 13%; eosinos. 2%. Slight leucocytosis with relative increase in the large mononuclear cells.

To-day further changes may be observed. Resolution has progressed so that the central areas of some lesions are now pale, smooth, and flat, being enclosed by hard almost verrucose cord-like margins forming rings and circinate patterns. The colour of the raised parts is a dull brownish red and is quite suggestive of hypertrophic lichen planus in the adult. The above photograph shows these features very well. During the last month a dense eruption has appeared on the trunk, affecting the back more than the chest and abdomen. This eruption consists of closely set, flat-topped reddish papules, oval or rounded, and in general morphology like small lichen planus papules but the tint is not lilac nor does the papule surface show the usual striae. No buccal lesions have been observed. The child's general health is deteriorating, and there is a steady loss of weight. She is being admitted to The Hospital for Sick

Children for observation. Since there is no history to support the diagnosis of a halogen eruption the provisional diagnosis is lichen planus and other opinions will be welcomed.

Discussion.—Dr. G. B. DOWLING said that if these lesions could be transferred to adult skin there would not be much hesitation in naming the condition lichen planus.

Dr. S. E. DORE said that the lesion looked like a bromide eruption, but the history was against that diagnosis, though histology seemed to favour it.

The PRESIDENT said that he also thought that the lesion was a bromide eruption.

Dr. MUENDE said that in his first report he had said that the condition was most suggestive of bromide eruption, but a closer inspection had led him to change his mind.

Dr. HUGH GORDON said that some of these lesions had begun as deep-seated vesicles. The case reminded him of one that he had shown at the meeting held in February¹, in a small child who had lichen planus atrophicus on the forearms. These lesions had begun as deep-seated vesicles which, when they subsided, left scarring and presented a similar appearance to that in the present case. He thought that the condition in this case also might be a type of lichen planus.

Dr. W. N. GOLDSMITH said that when he had seen the case at St. John's Hospital he had suggested that the condition was xanthoma. The tumours on the limbs were larger than any he had seen in a bromide eruption. Moreover there was complete absence of pustulation. There was, however, a curious translucency of the superficial part of the tumours, but they were quite solid. The case reminded him of one he had shown at a meeting of the Section some years ago (*Proc. Roy. Soc. Med.*, 1932-33, 26, 747), that of an infant having large, hard, red tumours, some of which ulcerated and fungated. Dr. Whitfield and Dr. Parkes Weber considered that case to be the type described by Dr. J. E. R. McDonagh (*Brit. Journ. Derm. and Syph.*, 1912, 85), as naevo-xantho-endothelioma. This was confirmed histologically, there being a very large number of Touton's giant cells present. The histological section of Dr. Brain's case was, however, rather different. There were only a few not very typical giant-cells. A point made by Dr. McDonagh was that fat only made its appearance at a late stage in the evolution of the tumours, and he thought it a secondary fatty degeneration of a primary endothelioma. It would be worth while staining further sections for fat.

¹ *Proceedings*, 1937, 30, 736 (Sect. Derm., 46).

[The report of other cases shown at the meeting will be published in the next issue of the PROCEEDINGS of the Section.]

Section for the Study of Disease in Children

President—C. PAGET LAPAGE, M.D.

[April 23, 1937]

Tuberose Sclerosis with Rhabdomyomata in the Heart: Pathological Specimens.—ELIZABETH O'FLYNN, M.R.C.P., and HELEN M. M. MACKAY, M.D.

Specimen from J. J., male, aged 8½ months.

Family history.—Only child. Parents said to be healthy and not blood relations. No family history of fits, mental deficiency, or adenoma sebaceum.

History of patient.—At 2½ months brought to the Queen's Hospital for Children on account of poor progress (had gained about ½ lb. since birth), crying, and some vomiting. History of probable fits when 1½ months old. Thin, underfed infant with very hypotonic muscles; usually lying with the head retracted; rather narrow barrel-shaped chest, and marked asymmetry of head and chest. Respiration rate variable, usually rapid. The right border of the heart could not be defined satisfactorily by percussion, on account of the chest asymmetry and the marked bulging of the ribs to the right of the sternum. Skiagrams showed a large shadow extending to the right of the mediastinum—evidently due to the thymus (fig. 1), since subsequent skiagrams showed its gradual disappearance (fig. 2). In right infra-axillary region, impaired percussion note and weak breath sounds. Ophthalmoscopic examination negative. There were minor epileptiform attacks without cyanosis.

Cerebrospinal fluid: No abnormal findings.

Subsequent progress.—The child at first noticed his surroundings, but progressive dementia developed. At 7 months he weighed 11½ lb., and appeared to be blind. Epileptiform attacks occurred daily. There was a convergent strabismus, extreme hypotonus of limb muscles, but no paralysis. Respiration rate usually 40–60, pulse-rate 130–160, temperature normal to 101° F. The retracted head looked large on the undersized body, but there was no separation of the sutures; head circumference 17½ in. Skiagrams now showed disappearance of the thymic shadow and enlarged right heart (fig. 3).

When 8½ months old child died, with symptoms of pneumonia and a temperature of 105° F.

Post-mortem examination, performed twenty-four hours after death (Dr. Elizabeth O'Flynn).—The body was that of a wasted infant, with marked asymmetry of head and trunk. The right side of the head and the right ear were more prominent than the left. The right chest bulged anteriorly and laterally, and formed a definite convexity to the right. No abnormality of skin.

Chest.—Lungs: Right showed patch of consolidation in lower lobe; left showed partial collapse. Thymus not enlarged. Heart and pericardium (weight 52 grm.); considerable hypertrophy and displacement to right. Small whitish elevations present on anterior surface at junction of right and left ventricles. Heart cavities: In the right ventricle two small nodules were seen projecting into the upper part of the cavity from the region of the attachment of the left tricuspid valve and the adjoining

part of the interventricular septum (fig. 4). The latter formed a firm rounded mass projecting into the cavity. Embedded in the septum were an ovoid mass about $1\frac{1}{2}$ cm. long, and several smaller ones; their pale colour distinguished them from the

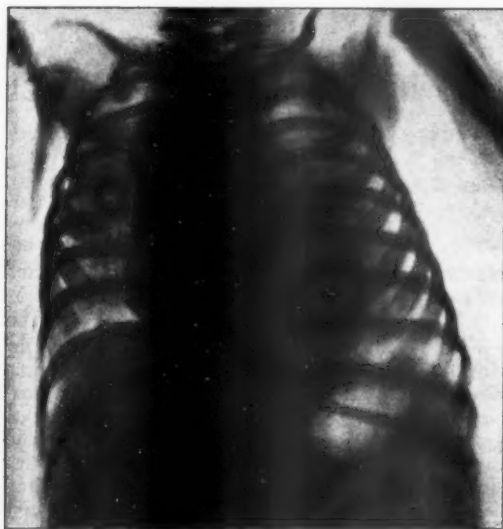


FIG. 1.—2½ months old. Thymic shadow to right of mediastinum.

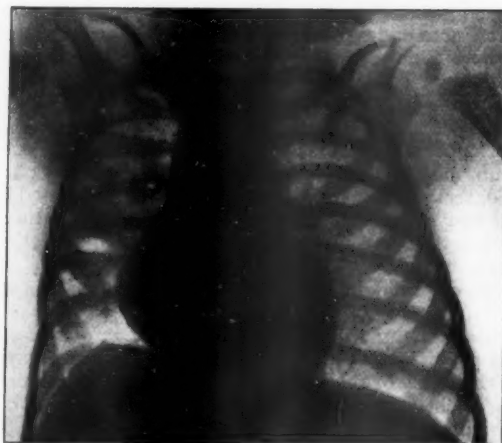


FIG. 2.—5½ months old. Thymic shadow much smaller. Outline of enlarged heart now obvious to right of sternum.

rest of the muscle. A small nodule was present in the left ventricle. The walls of the ventricles were much thickened, the cavities relatively small. Vessels appeared normal.

Abdomen.—Liver, spleen, and intestines, appeared normal. Kidneys showed no tumour formation. Suprarenals normal.

Brain.—The hemispheres were asymmetrical; the right measured 16½ in., frontal to occipital poles; the left measured 14 in. The convolutions varied considerably in

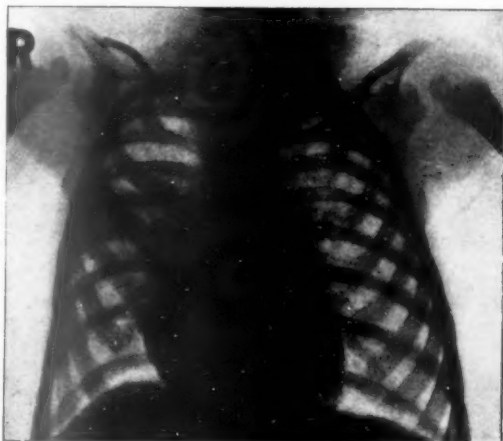


FIG. 3.—7½ months old. Thymic shadow almost disappeared. Band of shadow extends outwards towards right axilla (area of collapsed lung found at post mortem in this region).

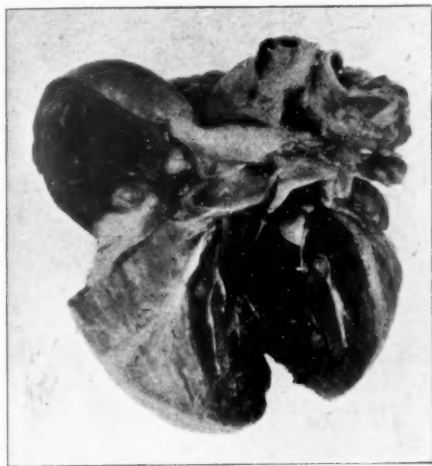


FIG. 4.—Heart—large mass occupies the interventricular septum. Smaller nodules project into the cavities.

size, colour and, especially, in consistency, some soft and normal, others whiter, rounded, and rubber-like. The harder areas outnumbered the more normal areas and showed no regular distribution. On section, in addition to the above, numerous

small tumours were seen under the ependyma and projecting into the cavity of the ventricles, especially the third (fig. 5). The cerebellum, brain-stem, and cord looked normal. Slight hydrocephalus.

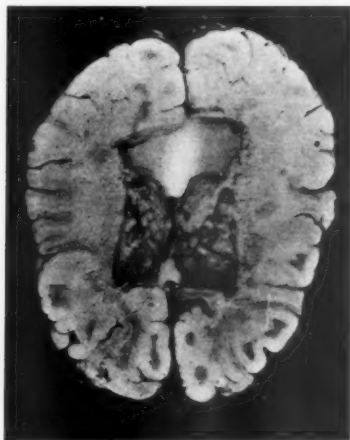


FIG. 5.—Brain. The sclerotic areas are white; the degenerated sub-cortical areas dark.

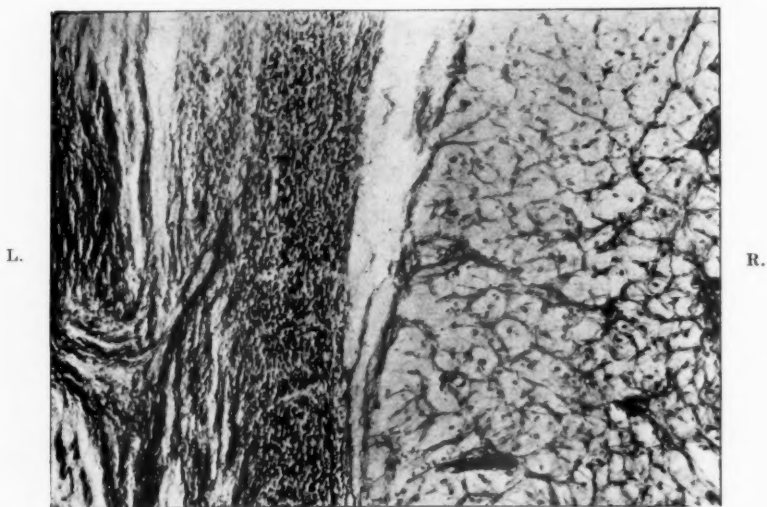


FIG. 6.—Low power view of tumour, on right, sharply delimited from the normal heart-muscle on left.

Histologically.—Rhabdomyomata: The pale areas are sharply defined by a fine capsule from the surrounding muscle. Those projecting into the ventricles are covered by endothelium. Under low power they appear to consist of a sponge-like

tissue with empty spaces of various sizes (fig. 6). By special staining the tumour cells are seen to contain one nucleus relatively rich in chromatin. The cytoplasm is irregular, with a centrally placed mass, from which come off numerous fine cytoplasmic prolongations in all directions. The interstices between these prolongations appear empty; in some, however, well-marked striations are present, and the resemblance to normal heart muscle is very definite (fig. 7). The striation is sometimes best seen in the periphery of the cell. In the smaller nodules there is less differentiation, the cells are more empty, the nuclei often missing. No fat, lipid or glycogen is demonstrable by special technique.

The changes in the brain are similar to those described by various writers (Brushfield, Wyatt, Friedman), and consist of a patchy gliosis of the cortex and softening of the subcortical white matter.

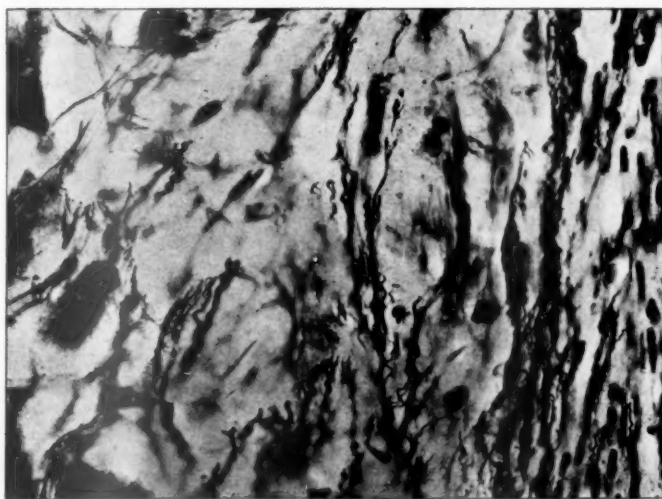


FIG. 7.—High power view of tumour showing striation.

Microscopically there is marked glial overgrowth; glial cells at various stages of development, from small round cells to the more mature fibre-forming type, are present.

Here and there are to be seen clusters of large ganglion-like cells. These may be abnormal glial cells, nerve-cells, or some form of reactionary giant cells; their nature is quite unknown. Nerve-cells, &c., and concentric bodies, ? psammomas, can be seen.

No histological changes were discovered in other parts of the nervous system examined, including brain-stem, cerebellum, and cord.

The main interest in the pathological picture lies in the tumours of the heart. Their nature is still in doubt, but there is good evidence that they consist of heart-muscle fibres, which have retained their embryonic character up to a point, and then undergone some form of degeneration. It is well known that fibrous tumours are found later in life, also associated with tuberose sclerosis, which are evidently the remains of rhabdomyomata of earlier years.

Dr. Helen Mackay drew attention to two phases in the child's clinical history. When he was 2½ months old attention was concentrated on the child's thinness, his rapid breathing, often with recession, on the abnormal shape of the head and chest, and on the shadow shown in the skiagram to the right of the sternum. Two of her (Dr. Mackay's) colleagues quite rightly maintained that the shadow was due to the thymus, but at this stage she had thought she was possibly dealing with an intrathoracic tumour causing pressure symptoms, with or without an enlarged heart. The forward bulge of the ribs to the right of the sternum seemed to favour this idea. In contrast with this was the final phase about six months later: a wasted, 8 months' old infant, taking no notice of anything, who lay with flaccid limbs and retracted head and suffered from numerous myoclonic twitchings and epileptiform attacks without cyanosis. There was internal strabismus. Breathing was still rapid, but at this stage the thymic shadow had disappeared, and the skiagram showed an obviously enlarged heart.

The condition was not diagnosed in life. The dementia developed much too rapidly to be the result of fits. Possibly the progressive dementia, epileptiform attacks, and enlarged heart with rapid breathing, in an infant of very poor physical development, might have suggested the true diagnosis to someone who had previously seen this syndrome. Tuberosc sclerosis has been described in an infant only 2 days old, and it has been stated that in 50% of all the cases there are fits in the first year of life. Nevertheless it has rarely been diagnosed in life at this early age. In older children and in adults the presence of adenoma sebaceum on the face might make the diagnosis easy, and this eruption has been observed in infants of 9 weeks, 6 months, and 13 months old respectively, so that occasionally a definite diagnosis should be possible in infancy.

Tuberosc sclerosis was an extraordinary condition. Steward and Bauer (1932) gave the following remarkable list of tumours found with this disease: tumours in "brain, ependyma, kidneys, heart, skin, pancreas, intestine, thyroid and mammae", which might be "undifferentiated embryonic neoplasms, gliomas, hæmangiomas, lipomas, myomas, fibromas, mixed tumours, teratomas, dermoid cysts, or carcinosarcomatodes". To this might be added tumours in retina, spleen, and lungs (Lind 1924), and also congenital abnormalities: spina bifida, cystic kidneys, supernumerary digits, syndactylomy, hemihypertrophy and pigmentary changes in the skin (Critchley and Earl 1932). Granting that a few of these associations might be due to chance, what could be the underlying condition giving rise to such diverse conditions?

REFERENCES

- CRITCHLEY, M., and EARL, C. J. C. (1932), *Brain*, **55**, 311.
 LIND, W. A. T. (1924), *M. J. Australia*, **2**, 290.
 STEWARD, H. L., and BAUER, E. L. (1932), *Arch. Path.*, **14**, 799.

Dr. PARKES WEBER said that the present case was important in regard to the clinical diagnosis of tuberosc sclerosis in infants. In older children the clinical diagnosis was often extremely easy, owing to the presence of conspicuous red, telangiectatic, sebaceous adenomata (Pringle's nævi) on the face. Indeed, when the latter were combined with a history of occasional epileptic fits the clinical diagnosis of tuberosc sclerosis was almost certain. Their association, not with tuberosc sclerosis, but with meningeal nævus, was extremely rare, if not unique (D. M. Greig, *Edinburgh M. J.*, 1922, n.s., **28**, 105).

Chronic Sinus of Face.—A. SIMPSON-SMITH, F.R.C.S.

W. H., male, aged 10. Referred by Mr. H. Pace Gibb.

Sinus underneath right lower eyelid, of three years' duration.

First seen by me two years ago. Cultivation of discharge showed no tubercle bacilli but moderate growth of *Staphylococcus albus*.

Skiagram (Dr. Horace Post) shows "a little bone sclerosis of maxilla underlying position of ulcer and probably due to this."

Wassermann and Kahn reactions negative.

Sinus curetted. No bare bone.

June 1935: Readmitted to hospital. Sinus area again opened. More extensive search for diseased bone negative. Curetting of track and excision of edge.



Chronic sinus of face.

Report (Dr. R. R. Elworthy): "A deep infolding of the epidermis, surrounded by subacute inflammatory tissue." Wound broke down.

July 1935: Readmitted. Stereoscopic X-ray examination negative. *Skiagram* of track after lipiodol showed extension almost to the ear on outer side of facial bones.

One year later: Sinus still discharging; no improvement.

Advice is now sought as to appropriate treatment.

Hepatomegaly. ? Cause.—G. H. NEWNS, M.D. (by courtesy of Dr. E. A. COCKAYNE).

L. D., male, aged 5½, has, according to the parents, always had a large abdomen. For six months past he has been getting thinner, though his appetite is good. He is inclined to become breathless on exertion. No illnesses of note.

Family history.—Three other children, healthy. Parents not blood relations.

On examination.—Height 40 in., weight 32 lb.; both below average. Rather backward mentally. Normal facies. No telangiectases. Heart normal. Both lungs normal except for scattered rhonchi. Abdomen considerably distended;

circumference at umbilicus 25 in. A large tumour occupies most of the right side of the abdomen, and extends upwards beneath the costal margin and down into the iliac fossa. An edge can be felt but it runs almost vertically downwards into the iliac fossa. No ascites. Stools normal. Acetone has only occasionally been present in the urine.

Investigations

Blood-count: R.B.C. 3,010,000 per c.mm.; Hb. 65%; C.I. 1.0. W.B.C. 6,800 per c.mm. (polys. 50%, lymphos. 34%, monos. 14%).

Blood-sugar:

Minutes after adrenaline	...	0	5	15	30	60
Blood-sugar mgm. %	...	74	90	88	100	110

Lævulose tolerance test:

Hours after 19 grm. lævulose	$\frac{1}{2}$	1	$1\frac{1}{2}$	2
Blood-sugar mgm. % ...	81 (fasting)...	107	84	90	98

Sedimentation rate: Thirty mm. in one hour.

Skiagram of abdomen: Right kidney outline visible and not enlarged; calyces filled with uroselectan.

Discussion.—Dr. HELEN MACKAY said that in those cases of von Gierke's disease which showed spontaneous improvement and perhaps cure, the disappearance of the metabolic disorder would presumably be accompanied by the disappearance of acetone from the urine, and the appearance of a normal blood-sugar response to adrenaline injection. Hence one would expect to find cases of von Gierke's disease in which the liver was still enlarged, but in which there was no biochemical evidence in blood or urine of active metabolic disorder.

Dr. PARKES WEBER said he thought, that, even if no "biopsy" examination of the liver by hepatic puncture were made, the subsequent clinical course would show whether the case was one of Gierke's "glycogen storage disease" or not. In Worster-Drought's case (*Brit. M. J.*, 1933, (i), 403), no puncture of the liver was made and the patient practically completely recovered, but there could hardly be a doubt about the diagnosis.

? **Gargoylism (Chondro-osteo-dystrophy).**—J. B. L. TOMBLESON, M.D. (introduced by Dr. E. A. COCKAYNE).

Brian T., male, aged 2 years 7 months. Birth-weight 9¾ lb. Fed on Nestlé's milk. Abnormality noticed since age of 4 months. Taken to hospital in Wales where the case was thought to be one of cretinism and was treated by thyroid. Later the child was treated in London, on the possibility of his being a cretin, but with no benefit as regards mental development, which was definitely retarded.

Family history.—Parents normal and not blood relations. Four other children, two brothers, aged 16½ and 12, the latter of whom has chorea, and two sisters, aged 8¾ and 6.

4.2.37: Admitted to Highgate Hospital on account of severe irritability and continual screaming. Bowels constipated.

On examination.—Pale. Flabby musculature. Head large, and long antero-posteriorly, with bulging of lower part of temporal bones. Depressed bridge of nose. Face large, with coarse features. Purulent nasal discharge. Head circumference 20½ in. Teeth: 8 incisors, and 1 left lower molar erupting; all show signs of caries. Corneæ clear, fundi normal. Abdomen protuberant, with large umbilical hernia. Liver and spleen not felt. Both testicles in the scrotum and of normal size. Downy hair on back.

Mentality.—Fairly bright, notices things around him, plays with pennies, putting them into and taking them out of purse. Appears to see and hear quite well. Can stand with support, but cannot walk or talk.

Skeletal system.—Marked lumbar kyphosis. No joint swellings. Slight limitation

of extension of knees, and plantar flexion at ankles. Stands with thighs slightly curved forwards and knees slightly bent.

Radiological examination.—Skull large, with gaping sutures and open anterior fontanelle. Sella normal. Spine shows wedged second lumbar vertebra, causing angular kyphosis. Radii show recently arrested growth line; otherwise normal. Femora and tibiae slightly thickened. Metacarpals and metatarsals normal.

Blood.—Blood cholesterol 87 mgm. per 100 c.c. serum. Blood phosphorus 5 mgm. per 100 c.c. Blood calcium 11.1 mgm. per 100 c.c. Wassermann and Kahn reactions negative.

Blood-count (30.3.37): R.B.C. 4,290,000; Hb. 68%; C.I. 0.79.

Sugar-tolerance curve rather flat.

Discussion.—THE PRESIDENT said he thought the case showed signs which pointed to some degree of cretinism. The chief amongst these signs were the protruding tongue, the prominent umbilicus, the hoarse cry and the featural configuration.

Dr. P. R. EVANS said that a case had been shown at a meeting in 1936 (*Proceedings*, 1936, 29, 500), as “? Cretinism: with upper lumbar kyphosis resembling that in Morquio's disease.” There had been a deformity of the second lumbar vertebra similar to that in the present case, and this occurred in both Morquio's disease and gargoylism. The patient had improved with thyroid treatment, which was discontinued after six weeks, and for a time the improvement had been maintained. Subsequently the patient relapsed and thyroid treatment had to be resumed.

Dr. PARKES WEBER, in regard to the diagnostic value of a wedge-shaped vertebral body, pointed out that a wedge-shaped vertebra was present in most cases of congenital (“osseous”) kyphosis or scoliosis.

Werdnig-Hoffmann Paralysis in the Elder of Twins.—C. HARDWICK, M.B. (for Dr. DONALD PATERSON).

A female infant, the elder of binovular twins, born December 19, 1936, by a normal labour at term. Birth-weight $4\frac{1}{2}$ lb. Fed first on Nestlé's milk and then on half-cream Cow-and-Gate milk.

Family history.—Parents both healthy and not related. Three other children, one of whom died soon after birth. No miscarriages.

Present illness.—It was noticed from birth that the child breathed rapidly, with short shallow respirations. The maternity nurse revisited her at the age of about seven weeks and noticed that she could not move her arms and had a greatly distended abdomen. She was admitted to Great Ormond Street Hospital, under the care of Dr. Paterson, a few days later.

On examination.—Somewhat wasted; cried feebly; distended abdomen; diaphragmatic respiration with indrawing of the lower intercostals. Did not attempt to move arms or legs; thigh and upper-arm muscles flabby and wasted. The hands and feet would move. When she was held up on the palm of the hand her head fell back and her legs dropped down. No reflexes obtained. Heart sounds normal. Fundi oculi normal.

The other twin was examined and found to be quite normal.

The baby was in hospital for three weeks and during this time gained 10 oz. in weight.

Postscript.—Since the date of the Meeting, she has died, at the age of 6 months.

FURTHER REPORTS OF CASES PREVIOUSLY SHOWN

Lipodystrophia Progressiva.—PEARSE WILLIAMS, M.D.

Previously shown 27.1.33 (*Proceedings*, 26, 515, Sect. Dis. in Child., 35).

B. K., female, aged $8\frac{1}{2}$ when first shown, is now aged 12 years and 10 months. 11.1.33: Height 48 in. Weight 47 lb., i.e. 7 lb. below average.

29.9.36 : Height 59½ in. Weight 105 lb., i.e. 13 lb. above average.

The following are extracts from the out-patient record :—

12.10.34 : Improvement in general health ; is gaining in weight and height.

14.5.35 : Ill during April with pneumonia ; treated at home. Legs, thighs, and buttocks well covered with fat but no fat on upper half of body.

25.2.36 : A little fat appearing on shoulders.



B. K., aged 8½ years.



Aged 12 years.

12.5.36 : Now nearly 12 years old. Breasts well developed. Excess of fat on thighs, buttocks, and lower abdomen. Fat deposit increasing on shoulders and upper arms, but absent over upper chest and face.

29.9.36 : Patient now complaining that she is too fat. Legs, thighs, buttocks, and lower abdomen are well covered. Upper abdomen, chest, and shoulders have a moderate fat layer. Face still lacks fat. She has had two normal menstrual periods.

An unusual feature is the development of fat over most of the previously affected part of the body. This case is also noteworthy in that the mother of the patient suffers also from the same maldistribution of fat, as may be seen in the clinical photograph.

Acholic Familial Jaundice in the Third (? Fourth) Generation of Manifestation of the Disease.—J. W. HANNAY, M.R.C.S., L.R.C.P. (for Dr. K. H. TALLERMAN).

I. S., female, aged 10.

Acholic familial jaundice diagnosed at the age of 9 weeks. Shown at the meeting in May 1927 (*Proceedings*, 20, 1582, Sect. Dis. in Child., 68).

Since then has attended the London Hospital at irregular intervals, remaining well, except for periodic attacks of jaundice, until November 1936, when she was admitted to hospital with a four days' history of headache, giddiness, vomiting, increasing jaundice, and dark urine.

On examination.—The child was deeply jaundiced and appeared very ill. Temperature 99–103°, pulse 128, respirations 28. Lungs normal. Heart: Apical systolic murmur. Liver not palpable. Spleen enlarged to within 1 in. of mid-line below the umbilicus. Urine: No bile. Stools dark.

Blood-count: R.B.C. 2,040,000; Hb. 46%; C.I. 1.15; W.B.C. 8,600; reticulocytes 20%. Fragility: hæmolysis to 0.55% saline.

Daily blood-counts on the following four days showed R.B.C. 1,900,000–2,400,000, and Hb. 41–49%.

The child's condition speedily improved. Six days after admission she was given a transfusion of 350 c.c. citrated blood. The following day splenectomy was performed by Sir James Walton.

Operation.—An enlarged spleen, weighing 1½ lb., showing no perisplenitis, was removed. The gall-bladder was normal and contained no stones.

Microscopical examination.—Spleen showed prominent Malpighian bodies with germ centres. Congested pulp with slight diffuse infiltration with eosinophil and neutrophil leucocytes, but no erythropoiesis. Moderate increase of free iron. One old and also recent hæmorrhages in trabeculae.

Blood-count the day following operation: R.B.C. 3,300,000; Hb. 65%; C.I. 0.98; W.B.C. 13,600; reticulocytes 33%. Fragility: hæmolysis to 0.6%.

The child made an uninterrupted recovery and was discharged well, four and a half weeks after admission.

Family history.—Father normal. Mother: Attacks of jaundice all her life until 1925, when splenectomy was performed. No attacks since. 1927, three months after the birth of this child, fragility still 0.55% hæmolysis.

Siblings: Two, and a half-sister (father's child) normal. One younger sister aged 4½, mildly icteric at times; known to be a case of family acholic jaundice, having a somewhat enlarged spleen and slightly increased fragility of the red cells.

Maternal grandfather: Attacks of jaundice all his life. Splenectomy with cholecystectomy (gall-stones) by Sir James Walton in 1931. Fragility 0.55%.

Maternal great-grandfather: Attacks of jaundice all his life. No further details available.

Pick's Syndrome (Pericardial).—J. M. VAIZEY, M.R.C.P. (for Dr. R. A. ROWLANDS).

This patient was shown by Dr. Stewart Wallace for Dr. Rowlands on October 25, 1935 (*Proceedings*, 29, 125, Sect. Dis. in Child., 7).

A. H., male, now aged 15. Admitted to London Hospital on April 22, 1935, with acute pericarditis. He had at that time an irregular pyrexia with tachycardia and a to-

and-fro murmur. No œdema, ascites, or hepatomegaly. After five weeks pyrexia subsided, but liver enlarged rapidly and signs of right pleural effusion appeared. During July 1935 abdominal paracentesis performed three times; right side of chest aspirated four times between July and October, 1935.

When last shown: Dyspnoëic on exertion. Congested cervical veins. Tachycardia up to 130 per minute. Signs of right pleural effusion and ascites. Heart not enlarged. Blood-pressure 125/90.

Pleural effusion and ascitic fluid both contained excess of lymphocytes. No organisms cultured. Guinea-pig inoculation negative. Electrocardiogram: Low voltage and flat T wave. Radiogram: Unusually straight left border to heart; no other abnormality.

Subsequent course.—Patient remained in hospital until January 26, 1936, and was readmitted on four occasions for aspiration of the right pleural effusion. Further abdominal paracentesis was not required.

On July 24, 1936: 3,200 c.c. of fluid was aspirated from the right pleural cavity and replaced by 2,600 c.c. of air. A radiogram taken then showed "heart only slightly enlarged in region of pulmonary arc in antero-posterior view. Right ventricle prominent in left oblique view, but very little pulsation on posterior aspect of the heart. The findings are compatible with adhesions obstructing the right pleural veins."

Since this time the patient has been attending regularly at fortnightly intervals, and has remained perfectly well. The pneumothorax absorbed and no further effusion formed. He is now at work and experiences no dyspnoea or distress. There is no œdema, no ascites, and no pleural effusion.

Dr. F. PARKES WEBER said he thought that this patient had suffered from some kind of "polyserositis", which latter, however, had not persisted, so as to give rise to "Pick's syndrome".

Cœliac Rickets.—H. J. SEDDON, F.R.C.S.

B. B., male, aged 16 years (May 1937), previously shown 28.10.32 (*Proceedings*, 26, 153, Sect. Dis. in Child., 9).

15.2.33: Discharged from hospital after treatment previously recorded, wearing outside steels.

7.6.33: Splints discarded. Instructions regarding diet have been completely disregarded.

3.5.37: *Follow-up examination.*—Small but healthy-looking boy. Height 53½ inches, weight 81 lb. Intelligent and cheerful. Muscular development subnormal, but said to be improving. Walks with a waddle but can manage several miles without fatigue. Abdomen slightly prominent, not doughy in consistency. Slight atrophy of buttocks. Funnel deformity of chest unchanged. Femora bowed; genu varum 4½ inches; 15° limitation of extension in left knee; full movement in other joints. Slight clubbing of fingers. Epiphyses still slightly enlarged. Skiagram shows that the rickets has barely healed.

Fæces: Total fat 31.7%, unsoaped fat 13.3%, neutral fat 5%, free fatty acids 8.3%, combined fatty acids 18.4%. Microscopic appearance normal.

Other investigations not possible.

Section of Urology

President—BERNARD WARD, F.R.C.S.

[March 23, 1937]

Renal Pelvic Epithelioma with Massive Calculi and No Infection.—

A. WILFRED ADAMS, F.R.C.S.

History.—M. A. F., male, aged 65, first seen in February 1937, stated that for thirty years heavy bouts of symptomless hæmaturia, lasting about three days, had occurred every year or two. His extremely timid disposition helps to explain this surprising duration. Two years ago niggling pain set in along the left loin and his health began to decline. Since then he has lost 3 stones. One month ago anorexia, vomiting, and constipation began and hæmaturia became continuous.

Examination.—This showed a wasted despondent man, with a high colour—which is remarkable in view of the nature of his complaint. Pulse, temperature, and respirations were normal. The abdominal skin was very inelastic. The left flank was filled by an almost painless, very firm lump, suggestive of renal swelling, and about the size of a coconut. It was disconcerting to feel its heterogeneous consistency, with stony areas by the ribs and irregular elastic swelling of the surface at the lower pole. Across it the colon was easily palpable.

Skiagrams (fig. 1) provided a great surprise, in the form of opacities, looking like barium, all along the left half of the colon. (The patient had been taking bismuth.) Repeated enemata effected no change in this appearance and compelled the conclusion that the shadows were due to constituents of the renal swelling. The soft tissue outline of the right kidney was normal, but it was difficult to assess how far a secondary nephritis in it was responsible for the obvious uræmia.

From the data obtained up to this stage in the proceedings, the following diagnoses claimed differentiation but none of them quite fitted the story, viz. calcareous deposits in tumour, tuberculosis, polycystic disease or primary massive renal calculi. It seemed fair to explain the situation to him and he was told that the only possible way to escape bleeding to death lay in operation, and the chance of success was very remote. Faced with this dilemma, he accepted the operation which for too long he had dreaded.

Urological investigation.—Excretory pyelography showed one or two small shadows, possibly of uroselectan, in the right renal area.

Cystoscopy demonstrated that the hæmaturia was derived solely from the left ureter. Urine from the right side gave urea 1.8% and from the left, 0.8%. That from both sides was sterile and the only abnormal constituent was a large number of red blood-cells in that from the right ureter and a very large number in that from the left.

Discussion and Pre-operative Diagnosis.—(1) (a) Calcareous infiltration of tumour. The diffuse extent and density of the shadows was out of keeping with the patchy



FIG. 1.—Massive nephrolithiasis (left).

calcifications occasionally found in neoplasms. The long history of thirty years seemed incompatible with malignant disease.

(b) Obsolete tuberculosis. As hæmaturia had been the sole symptom, and the pathological findings in the urine were so negative, I rejected this diagnosis.

(c) Polycystic disease. The heavy intermittent hæmaturia, the unilaterality of renal involvement, and the diffuse extent of the opacity were opposed to this.

(2) Massive renal calculi seemed to be the likeliest diagnosis in the end. The acceleration of the patient's decline during the last year or two I attributed to increased hæmorrhage and depressed function in the opposite kidney.

Final diagnosis.—It was only when the swelling was explored that its nature became known. A double diagnosis was the true explanation as, complicating the calculi, there was a scirrhus mass in the renal pelvis, about two inches in diameter, adherent to the tissues around the vertebral column, from which it was cut off. The patient succumbed three hours later.

On section of the kidney calculi and gravel were found filling the dilated calices. In the specimen (fig. 2) multiple warty nodules are seen on the lining of the pelvis,



FIG. 2.—Section of left kidney showing calculi, gravel and scirrhus carcinoma of pelvis.

the wall of which is infiltrated, to a depth of about half an inch, with dense scirrhus growth, which Dr. A. D. Fraser describes as epidermoid carcinoma with evidence of rapid growth.

Conclusion.—The case arrests attention because symptomless hæmaturia over thirty years is an astonishing history for renal calculus while, from the ætiological standpoint, it also compels the conclusion that renal calculus is an insidious cause of carcinoma of the renal pelvis, even in the absence of infection.

Specimens from Three Cases of Ureterocele.—H. P. WINSBURY-WHITE, F.R.C.S.

I am presenting these specimens of ureterocele associated with lithiasis as examples of the influence which urinary stasis has on calculus formation. I need only say that in three out of four cases of ureterocele which have passed through my hands, stone was present, to emphasize the importance of this association. These cases are interesting not only from the scientific point of view but because they raise problems in treatment which vary in the respective cases.

The first patient was a married woman aged 38 who complained of attacks of pain in the left side and frequency of micturition during the previous two years. Cystoscopy showed a small but definite ureterocele in relation to the left ureteric orifice. A plain X-ray film showed two stones each about the size of a filbert in the left ureter, just outside the bladder. The intravenous urogram showed a moderate degree of dilatation of the lower ureter and only a slight dilatation of the corresponding kidney which appeared to be functioning well.

Destruction of the ureterocele by electrocoagulation failed to induce the stones to pass. They were obviously held up by a narrowing of the ureter where it joined the bladder. It therefore became necessary to cut down extraperitoneally on to the lower end of the left ureter, remove the stones, and re-implant the ureter into the bladder through another opening. The patient made a good recovery.

The second patient was a man aged 23 who complained of pain in the left side and of hæmaturia. Cystoscopy, in this case also, showed a ureterocele in relation to the left ureteric orifice. A plain skiagram showed a small collection of stones, obviously in the ureterocele, and two small stones in the lower pole of the left kidney. Because of the collection of the calculi in the sac in the bladder I decided on an open suprapubic operation, and excised the sac with its stones. I had hoped that the two small renal calculi, which were not too large to pass spontaneously, would ultimately make their escape, but a plain skiagram taken a year later showed these stones still present, and a little larger. They will be removed by open operation.

The third case was in a woman aged 36 who had been having attacks of fever accompanied by pain in the left loin over a period of six months. I believe she had also had chronic *B. coli* infection of the urine for the past ten years. Cystoscopy showed a moderate-sized ureterocele involving the left ureteric orifice. A plain X-ray film showed what appeared to be a stone, about the size of a filbert, in the region of the lower pole of the left kidney. Intravenous urograms showed a considerable degree of dilatation of the pelvic portion of the left ureter giving a shadow on the film of about one and a half inches in diameter. The kidney was only moderately dilated and was functioning fairly well. The urine in this case was heavily infected with *B. coli*. The X-ray appearances suggested that it might ultimately be necessary to remove the left kidney or, at any rate, to remove the stone from its lower pole. I felt that the best preparation for any operation on the upper urinary tract was to destroy the ureterocele through a cystoscope; by this means improved drainage would offer a considerable reduction of persisting sepsis. Under a general anæsthetic, I divided the ureterocele completely in a transverse diameter.

About five months later X-rays showed that the shadow previously seen in the kidney had completely gone, showing that it was a collection of sand rather than of stone. The ureter had considerably shrunk in size and cystoscopy failed to show a ureterocele. The left ureteric orifice appeared merely to be somewhat dilated. Urine collected from each kidney separately was clear, that from the left being a little paler than that from the right. There was no pus in either specimen but a few *B. coli* were detected from the left kidney. There was a good deal less urea in the specimen from the left side compared with that from the right.

While the patient continues to be well and the left kidney is relatively free from infection there is no indication for operative interference.

Large Ureteric Calculus.—CLIFFORD MORSON, F.R.C.S.

R. H., a girl aged 12, was admitted to the Hampstead General Hospital, in February 1937, suffering from painless hæmaturia.

History.—In 1930 she had been treated for tuberculosis of the left hip. After being kept in the decubitus position for twelve months she fractured her right femur

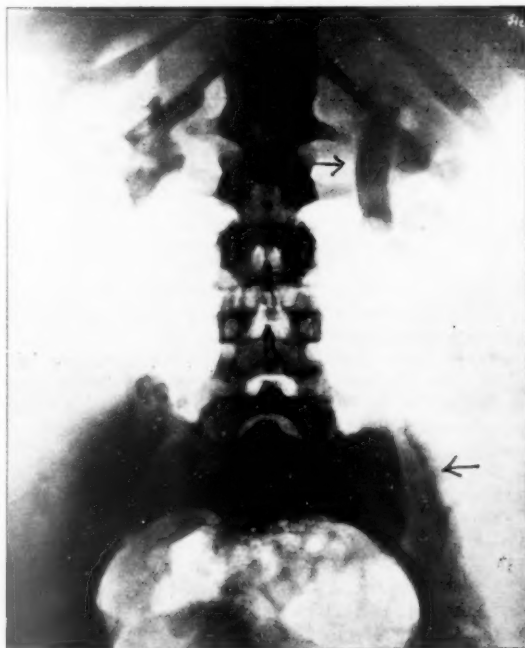


FIG. 1.—Intravenous pyelogram showing hydronephrosis of left kidney and large ureteric calculus, the lower half of which is opposite the sacro-iliac joint.

when getting out of bed. This accident necessitated a further period of confinement to bed. In 1934 calculi had been removed from both kidneys at a hospital in Plymouth.

On examination.—Investigation by intravenous pyelography showed hydronephrosis of the left kidney and the shadows of a stone in the upper end of the ureter and of another opposite the left sacro-iliac joint (fig. 1). These were removed by operation, from which the patient made an uninterrupted recovery. The lower end of the stone removed from the upper portion of the ureter was faceted and accurately fitted the upper end of the stone removed from the lower half of the ureter. At one time therefore these two stones were one and at a recent date had been fractured.



↑ site of fracture
FIG. 2.—Photograph of ureteric calculus 10 cm. in length.

Chemical analysis showed that these calculi consisted of calcium phosphate. The two stones joined together were ten centimetres in length (fig. 2).

It is well known that when patients are kept in the decubitus position over long periods infection of the urinary tract develops and calcium phosphate calculi are formed. It has been shown that there is loss of calcium from the bones in these cases. This fact and stasis of urine in the renal pelvis, due to immobility, account for the formation of the calculi. An additional factor is exposure to the sun's rays, which leads to concentration of urine.

Stasis in the urinary tract can be avoided by altering the position of the patient from time to time. This can be done by the use of the apparatus introduced by Dr. W. T. G. Pugh, the Medical Superintendent of the Children's Hospital at Carshalton.

Section of Psychiatry

President—T. A. ROSS, M.D.

[April 13, 1937]

Mental Disorder Following Head Injury

By C. P. SYMONDS, M.D.

THE outstanding feature of mental disorder after head injury is loss of consciousness in some degree. I add the qualification because a good deal of confusion is apt to arise in practice about what loss of consciousness means. It is argued quite reasonably that a man who is capable of answering questions, for instance, giving his name and address after an accident, is conscious. But if next day he has no recollection of having done so, or of the period of time when the incident occurred, he may with equal reason be said to have been unconscious of what he was doing. For purposes of description in head injuries, if a man has no memory of what he has done, we assume that he was not at that time fully conscious. Therefore, the duration of unconsciousness may be measured by that of the traumatic amnesia following the accident. It is the symptoms which may be observed during this period of traumatic amnesia that I shall first discuss.

Let us consider the common case of minor injury—one of so-called concussion. The clinical picture in the moment after the accident is dominated by the physical state of complete flaccid paralysis. The mental state is that of profound stupor. From this the recovery of consciousness may be rapid, but however rapid, it is always gradual. There is a transition from deep stupor to a state of dazed bewilderment, and after this automatism, before full consciousness returns, and the amnesia will often be found to include some utterance or action which has appeared "conscious" to the bystander. The whole process of recovery may take only a few minutes. Sometimes, even though the initial deep stupor may have been of momentary duration, the process of recovery may be spread over a longer period. In particular is this true of the phase of automatism, as in the well-known instances of football players who play to the end of the game after an injury, with subsequent amnesia. Occasionally the loss of consciousness after injury may be delayed. The patient may then remember the accident and the events immediately following it, and after a few minutes, sometimes an hour or two, lapse into a state of automatism which lasts several hours. These are the common mental effects of minor injury.

Turning our attention now towards the other end of the scale, after an exceptionally severe injury, we may see the progress of recovery to full consciousness spread over a period of days, weeks, or even months.

Between these two extremes every gradation may be observed. The mental disorder in the one case may be dismissed as "after-effects of concussion", or in the other, dignified by the title of "acute traumatic psychosis", but I believe there is no essential difference between the two. The long-drawn-out cases, of course, offer the greatest opportunities for observation.

Following the classical paper of Adolf Meyer in 1904, no important study of the acute traumatic psychosis seems to have appeared in the English language until Schilder's contribution in 1934. In the interval, however, several valuable papers have appeared in Germany, notably that by Pfeiffer in 1928. My own observations

are regrettably incomplete, in that they are derived from occasional cross-sections of the illness rather than from continuous records. They have been selected from the notes of 16 cases in which the acute symptoms lasted from three weeks to fourteen months.

In the course of a prolonged traumatic psychosis, a more or less regular sequence may be observed in the stages of recovery. There is at first the phase of deep stupor, with muscular relaxation. This negative state is of brief duration. Following this, Schilder distinguishes three stages :—

- (1) Deep clouding of consciousness, with general resistiveness.
- (2) Clouding of consciousness, with disorientation, bewilderment, and helplessness.
- (3) After the clouding of consciousness has subsided, a state of Korsakow's psychosis.

This classification of the stages of recovery is, I think, of value, but the transition from one stage to another is gradual and subject to fluctuations. Moreover, as the greater part of the third stage is included within the period of traumatic amnesia, there is still during this stage impairment of consciousness according to the definition which I have proposed.

I prefer, therefore, to consider the traumatic psychosis as a whole, recognizing in its course the predominance, at one time or another, of certain features: In the early stages stupor, later, confusion; and, after confusion has faded into the background of the picture, defective memory for recent events with a tendency towards confabulation.

Before attempting to describe the symptoms of mental disorder in these cases of severe injury, I should like to make it clear that the material from which I shall draw comprises the notes of patients with closed injuries only. That is to say, no case has been included in which a compound fracture might have complicated the clinical picture by introducing the effects either of visible laceration of the cortex, or of infection. Even in closed injuries, however, we may encounter the clinical evidence of coarse focal lesions, for instance, hemiplegia or dysphasia. Such cases, also, I have excluded, my object being to present what appears to be the direct effect of injury upon the cerebral function as a whole.

After the initial stage of flaccid coma, there is usually a period of deep stupor, associated with restless bodily movements, such as turning over in bed, but without speech, and without any response to internal or external stimuli above the level of the simplest alimentary, excretory, or protective functions. This state of deep stupor rarely lasts more than a day or two. I have seen one case in which it persisted for no less than eighty-five days, but in this instance there was a right hemiparesis, and I think it probable that a coarse lesion of the left frontal lobe played a part in the clinical picture.

As the patient emerges from stupor he is, as a rule, excited, sometimes dazed and bewildered, and reacts in a resistive, irritable way to outside interference. He is wet and dirty and has to be fed. Often there is delirium, sometimes with an occupational trend. This state may continue for days, weeks, or even months, and there may be occasional relapse into stupor for as long as two or three days at a time.

Gradually, behaviour becomes quieter and speech more coherent, so that it is possible for short periods to engage the patient in conversation and learn something more of the mental content. The salient features at this stage are as follows :—

There is profound disorientation in space and time, with a tendency to interpret the surroundings in terms of past experience. There is defect of perception and inability to synthesize perceptual data. Memory and judgment are grossly impaired. Thought is constantly impeded by perseveration. Disturbance of the speech function is conspicuous. The mood is often elated and there is sometimes a push of talk resembling that seen in hypomanic states.

Ritchie Russell has drawn attention to the tendency shown by patients in this stage to give their age as much less than it really is, and to speak of long-past experiences as if they had happened quite recently. This tendency, I believe, is not uncommon. There is a far-reaching retrograde amnesia and the patient's attempts at orientation are influenced by this fact. There is also a tendency even at this stage to confabulate.

Case I.—As an example, I have a note on H. B., a man of 29, a motor salesman, whom I saw with Mr. Cairns at the London Hospital on the 30th day after his injury. He had been in a state of restless stupor from the first, his behaviour gradually becoming more reasonable and his speech more coherent. He was still at the time I saw him occasionally incontinent. Sometimes he recognized his wife and sister. Outgoing speech was fair but he was unable to write intelligibly. He obeyed the spoken, but not the written, command. There were no signs of any focal lesion. The past history showed that he had gone from his preparatory school to the Royal Naval College at Pangbourne, subsequently for a short period into the Royal Naval Reserve, then into the Mercantile Marine, and for the eight years previous to his accident had been in the motor trade. He had been married five years.

The following is an extract from my note of our conversation :—

"What is your name?"

"Baylis." (He spells it correctly and afterwards his Christian name, Hugh.)

"What is your age?"

"Nineteen and a half."

"Is that all?"

"That's all—all so far."

"You look older."

"That's all I am."

"Are you sure you are not 29?"

"No, quite sure."

"When is your birthday?"

"January 8."

I ask the house surgeon what is his real age and he tells me.

The patient overhears this and says: "You can't tell unless you check up. These people round here in the cabins, they should know I'm three nine twenty nine. I suppose one gets older a bit in the Navy. I suppose your life sophisticates you a bit really."

"Where are you?"

"Where? Oh! I see what you mean. I'm in the public school semi-past Rugger stage. That's to say I play fairly well but not well enough to be one of the big noises. I'm fairly average at sports—in fact fairly good. Cricket, bad, definitely I should say—on averages."

"Have you got a job?"

"Yes I'm chief cadet captain—in charge of a term. Each of us has charge of a term."

"Do you earn your own living?"

"Well a cadet captain earns his own living up to a certain extent."

"Are you married?"

"No, I'm not married. I shall be married shortly after I leave here. I expect very shortly afterwards."

"Can you drive a car?"

"Yes."

"Have you got one?"

"No, except my father's car."

"Where does he live?"

"Hampshire. He drives one of those old-fashioned touring cars known as the Hampton."

"Who is this?" (pointing to house surgeon).

"I don't know."

"What is his job?"

"Oh, a scout number one to you, to find things out in an intelligent way."

"How is life generally?"

"Oh, life is grand generally. I think we're nearly at the end of the war now. I think we'll all be glad about that."

Q "What year is it?"

"The fifth year of the war actually."

"What year is it?"

"The thirtieth thousand year of the world, 1930th really of the . . . of our . . ."

Following this, I spent some time over a neurological examination, examined him with tests for aphasia, and then returned to the question of his age and job. Again he insisted that he was 19, and at Pangbourne, giving me details of the life he was leading, which were, on the whole, consistent.

The difficulties in the sphere of perception and in the synthesis of perceptual data have been very carefully described by Schilder. They play a large part in causing the confusion. So also do perseveration, distractibility, and the inability to distinguish clearly between figure and background in the thought process.

Goldstein, in describing the principal forms of disintegration of function following cerebral lesions, has emphasized the following points. In the first place, there is a rise of the threshold for excitation. In the second place, any stimulus which surmounts the raised threshold and causes excitation expands abnormally and lasts an abnormal period of time. These are in fact the phenomena of raised threshold and over-reaction with which we are familiar in partial lesions of the sensory pathway at any level. At the level of mental function they are expressed in terms of defective perception and perseveration. As a third characteristic effect of cerebral damage, the performances of the organism are unduly influenced by external factors. Finally, performance is affected by a disturbance of the figure-background relationship. According to Goldstein, the essence of every mental event is the formation of a figure which stands out in relief against a background. In every thought process there is an active tendency towards such figure formation. The tendency is to select from a mass of more or less suitable material those elements which are suitable for a precise figure formation, and to reject those elements which are unsuitable. The rejected elements form the background. As the final result we have the figure standing out in relief against a background of related but irrelevant material. As the result of disease, the selective action breaks down. The formation of a precise figure then is interfered with by the emergence of loosely related material from the background. The attempt at thinking, therefore, can only result in a blurred figure formation.

These conceptions of Goldstein are, I think, helpful in the understanding of traumatic mental confusion. I shall refer to them again from time to time.

Perseveration in thought, word, and deed is certainly one of the most striking features in this stage. The following case is an example:—

Case II.—A man aged 67 had a fall when hunting. He was in a state of deep stupor for several days, subsequently excited and confused, but when I saw him on the 70th day after his accident he had for some time been quiet and easily managed, except at night when he was sometimes delirious. He was able to feed himself, but when he tried to shave became muddled. He had been up and out for short walks. There had been no incontinence for a month.

I found him alert, amiable, and ready to converse. He was completely disoriented. Thought and speech at the automatic level appeared normal but anything more difficult was impeded by perseveration. For instance, he expressed a desire to urinate but said he would wait till the end of my examination. I then suggested that he might get out of bed to pass water so that I might see him on his legs, but later altered this, asking him instead to walk across the room to the window. He did so, stood gazing out into the garden, remarked that it was a fine day, and, while still looking out of the window, in an automatic way let down his pyjamas and began to urinate on the floor.

Disturbance of the speech function in the stage of the mental disorder which we are now considering is a symptom which at once attracts the attention of the neurologist. It is at times so prominent as to suggest a focal lesion, but the dysphasia shows an improvement *pari passu* with the general mental disorder, and it would seem that we are dealing with a general disorder of cerebral function in which the function

of speech is naturally involved. Observation and analysis of the dysphasia, therefore may, by sampling the general mental disorder at a particular point, throw some light upon its nature.

After the first return of automatic speech, there is often a considerable push of talk in which words and phrases are well formed but unrelated to one another or to the circumstances—in fact a jargon. Then the spontaneous talk begins to have some general direction, though it is for the most part meaningless. It is apt to be concerned from time to time with some habitual activity or actual experience. At this stage the patient's attention can be gained for a moment or two. He will answer questions, name objects, and read aloud, but his responses are inaccurate and often so distantly related to the question or request as to seem quite at random. The following case provides some illustrations of what may commonly be observed:—

Case III.—A man aged 27 was found on the road after a motor accident in a state of flaccid stupor. I saw him at the end of thirty-six hours when he responded only to painful stimuli with generalized movements of withdrawal. His cerebrospinal fluid was clear and colourless, with a pressure of 135. Seen on the 10th day he was excitable, talkative and confused. He said "How do you do?" and "Good-bye" normally, but otherwise talked jargon continuously. When asked his age, he said "27" and, in reply to all subsequent questions, said "27". When I ceased to question him he began counting from 27 to 35. His response to spoken commands was uncertain.

Asked to name a box of matches, he did so correctly, but subsequently called a watch "watches". Next shown a bunch of keys, he called it "grey locks" and continued to give this name to all objects subsequently shown him.

On the 12th day his spontaneous talk, though still meaningless, contained frequent references to theatres and Paris. (After his recovery I found that he had been to a theatre in Paris during the week-end before the accident.) Shown a florin, he called it a two-theatre piece but later a two-florin piece. A box of matches he called a theatre, but handled it correctly, took out a match, lit it and blew it out.

At this stage, above the automatic level, speech showed little relation to external stimuli, the stream of thought being mainly directed by the prevailing trend of the delirium. When any response to external stimulus could be obtained it was influenced by perseveration.

On the 14th day, the spontaneous talk, still meaningless, had frequent reference to hotels.

His response to naming objects was as follows:—

Watch	Clock of the hotel.
Pencil	Pencil of the hotel.
Keys	Pencil of the hotel.
Electric torch	Pencil of the hotel.
Watch	Clock of the hotel.
One shilling	Clock of the hotel.
Handkerchief	Pencil of the hotel.
Box of matches	Pencil of the hotel.
Tobacco pouch	That's more than the clock of the hotel. I think it's your tobacco pouch.
Fountain pen	Clock of the hotel. Fountain pen of the hotel.

He then continued spontaneously:—

"I think I'm a great deal better in that I think I can go the whole hog." This he repeated six times and went on:—

"I think I've seen this before. I think I've seen the whole hog, and that I've been quite willing to see the whole hog. Don't you think so? Don't you think the think of the whole tell? Don't you think the way of the hotel. I should be quite willing to realize the hotel?"

I again asked him to name a box of matches. He did so correctly and said:—

"And I think if you ask me fairly, I think that quite fairly the box of matches will be very much beyond the power of the hotel."

On the 80th day he was much improved; recognized he was in hospital, and had some idea of having had an accident. There was still, however, a great deal of confusion, and defective comprehension and perseveration made continuous conversation impossible.

On the 153rd day I saw him again. In the meantime he had been ill with a femoral thrombosis. This time he appeared to know me, gave me a cheerful greeting and said:—

"I know you, you were the doctor at the last place I was at. What was that place by the way? It has some connexion with this place, hasn't it? Aren't they run by the same people?"

"My name is Symonds, Dr. Symonds."

"That's right, Dr. Symonds. I always think it looks bad not to know people's names."

"How are you?"

"I am very well now. I am really. I mean all my legs are perfectly intact, but these medical people won't send you out of hospital until you are ready to give the world kicks."

Later I asked him my name.

"Hedley Hart. No, Hedley."

"But I told you I was Dr. Symonds!"

"Yes, but didn't you say it was Hart too? No, well I'm bad there!"

"What is this place?"

"Hedley Hart I think they call it. It has been changed round a lot. It used to be another building. Do tell me your name?"

He named pencil, watch, matches, ring, pipe, hat and gloves correctly in this order, but then called keys: "hitches, a box of hitches", correcting it to keys when they were jingled.

His response to spoken commands was good if they were not too long or complicated.

His response to a written command was as follows: The written request was "Undo the second button of your jacket, and do it up again". He read this to himself slowly and with a puzzled expression, and after sixty seconds began to fumble with his buttons, eventually holding the appropriate one but getting no further. He then said: "I rather wondered if you meant your second jacket or my second jacket. Was it your bottom you meant or my bottom?"

This response shows very well many of the factors which contribute to the mental disorder. There is first of all the slowness of perception and the inability to synthesize perceptions, to see the picture as a whole. Then there is the incapacity for precise figure formation and the perseveration.

The sequence of thoughts here, I suggest, was as follows: The word "second" brought out of the background the other members of a series—top, bottom, and so on. Hence the tendency to read "bottom" for button, a tendency increased by the clang association. On a subsequent reading the word "button" became clear. The word "bottom", however, having intruded into the picture, persisted. Furthermore, as the patient held the paper, he thought of himself in the first person and myself in the second person. Hence, in the final thought there were two unprecise or blurred figure formations, the one containing "second" and "bottom", the other "your" and "my". Doubt now gave an interrogative direction to the thought process, two questions being formulated in his mind: "Do you mean second button or bottom button?" and "Do you mean your jacket or my jacket?" The first question was correctly solved. Before he spoke he had taken hold of the second button, and as he spoke he held it. It was the second question, therefore, which he now wished to propound: "Do you mean your jacket or my jacket, your button or my button?" But perseveration of material belonging to the first question interfered with the proposition of the second. Hence its final form. Thus what appeared as a dyslexia was a representation at one point of the total mental disorder, and throws some light upon the basic confusion of thought which characterizes this state.

Shortly after this the patient began to improve. Seen on the 183rd day he appeared normal. He was able to retain seven digits, made no mistake in the name, address, and flower test, after five minutes, and showed good judgment. There was no longer any trace of dysphasia. He has now been back at his work for two years and, from my own observation and the reports of his friends and business associates, his cerebral function appears to be unimpaired.

Comprehension of the written command seems generally to return later than that for the spoken command. This difference is probably due to the fact that the written sentence is less easily perceived as a whole than the spoken sentence. As another example of the defect, I quote from Case II:—

Given the written command in block capitals: "Take your glasses off and give them to me", he read it through to himself slowly and performed the action correctly. The next day the request was repeated, being written in script in the following form: "Take off your glasses and hand them to me." This he read to himself and then aloud, but substituted the word "gloves" for "glasses", looked at his hands and said: "But I haven't got any." I then erased the word "glasses" in script and replaced it in block capitals. Again he looked at his hands and said forcibly: "I haven't got any." I then underlined the word glasses and exhorted him to try again. This time he read aloud: "Take off your gloves and glasses and hand them to me", took off his glasses and put them on the table.

Here, again, we note the slowness of perception and the difficulty in perceiving the sentence as a unit or even the unitary significance of certain words. As a result of the first reading of the sentence with imperfect comprehension, the word "hand" was introduced into the material for figure formation. Hence, on the second reading, the tendency to substitute "gloves" for "glasses". We see also the perseveration of the word "gloves" even when the sentence was eventually understood.

The transition from the stage of confusion to that of the Korsakow state is a gradual one. There is a tendency always for the patient, even when he is confused, to confabulate when pressed for information. This tendency often persists at a time when his behaviour in relation to the hospital surroundings and his speech in simple conversation no longer show confusion. There remains, however, gross defect of memory, especially for the most recent events, imperfect orientation, and impaired insight and judgment. The confabulation may, as Russell has pointed out, lead to false accusations in relation to the accident, as in the following note made by Mr. D. W. C. Northfield in Case I.

The patient on the 45th day after injury showed very fair contact with his surroundings, was correctly oriented as to place and person, and only four days out in the date. He was then asked to give an account of his accident. The facts were that he had been found on the road unconscious, with his car overturned, near Leominster: was taken to the hospital there, and removed while still in a state of stupor to the London Hospital.

"Where were you when you had the accident?"

"Hereford. Just outside Hereford, and this motorist, thinking I was someone he knew, overtook me and drove me into the hedge. Fortunately, being an experienced driver, I was able to stand on the brakes and get clear of the man. I went into Hereford and reported the matter to the police, feeling frightfully groggy. I heard the day later that the motorist and the pedestrian after him were prosecuted; one got ten years... no ten weeks and the other fined £25, so they must have been well known by the police. I only had thanks from the police."

"What did you do after that?"

"Oh, I went to bed. It was about 8.30 p.m. and on the following morning I felt I couldn't get up and rang through for medical aid. A doctor came and said I wasn't to get up. I was down there for a fortnight and then came here. Then I thought of this place as it was the only hospital I had previously been in. It has a great reputation for efficiency, and I'm very glad I came."

"Do you remember all about the accident?"

"Yes, pretty well. I remember him hitting across me and standing on the brakes. As a matter of fact I made a fool of the fellow. I had a new car and could do plenty of things with it that you couldn't do with an old car, and I just left him to it. Anyone who is in the retail motor trade and cannot drive a car wants to be looked at badly. On the trade side it is quite different. Fellow doesn't get the opportunities. May be able to drive quite well but is a foolish driver."

"Which hospital were you in at Hereford?"

"Hereford Hospital, Bridgemount Road."

"You had a clear recollection of going to hospital?"

"Oh yes. I did that to cover myself. That was within five minutes of the accident and they were very glad I came along. After that I seem to have been a bit barmy in some ways. I was there ten days and have no recollection of being there whatsoever, and I put it down to the fact that I was smashed in the head and was foolish. I don't remember the Sister in the ward whom my wife tells me saw a lot of us."

The Korsakow state, according to Pfeiffer, is a constant feature of the later stage of every prolonged traumatic psychosis. This, I think, is true in the sense that there is a stage in which gross defect of memory for recent events remains, sometimes for a long period, the outstanding symptom. But these patients do not always confabulate. When pressed for information they sometimes react in a helpless, bewildered, or irritable manner. The associated mood and individual make-up are factors which are of importance in this connexion. The patient who is elated, and of an easy-going talkative disposition, confabulates readily.

The mood is, in fact, often elated in this phase, and spontaneous talk is plentiful—often boastful, in a childish way—as in the case from which I have just quoted. Actually, this patient after recovery proved to be a pleasant, easy-going personality, outspoken but not boastful or aggressive. Sometimes the mood throughout the whole psychosis is indifferent, sometimes there is a rather childish petulant depression. Elation however is the commonest abnormality.

The ending of the Korsakow stage is by no means clean-cut—one would not expect it to be so. After the tendency to confabulate has disappeared, there is usually a period during which euphoria persists, with defective insight and judgment, and with a variable but sometime gross defect of retention. Noticeable is the patient's refusal at this stage to admit that there is anything wrong with him and the light-hearted way in which he may refer to the accident, even though it may have involved the death of a relative or friend. The return of insight is an important landmark and may be taken to mean that the acute traumatic psychosis is at an end. For instance, a man whom I had seen on several occasions in the later stages of recovery had on each occasion declared himself thoroughly fit though showing evidence of slight confusion. Three months after the injury in answer to my question he replied :

"I feel thoroughly fit, but I realize now that when I last saw you I wasn't fit, or in a condition to judge of my fitness. Therefore I may be not quite a good judge now."

The prognosis for the acute traumatic psychosis, including the phases of stupor, confusion, and confabulation, appears to be good whatever its duration. The longest record I have is that of Case II, in which the patient, a man aged 67, still showed some confusion and grossly defective memory fourteen months after his accident, but in a month from that time was quite clear and, though showing a slight residual deterioration of intellect and personality, has since (during the past year) managed his own affairs and led a normal life.

It appears then that the pathological changes, whatever they may be, which are responsible for the whole sequence of mental disorder which has so far been described, are reversible, at any rate to the point of allowing restoration of function under normal conditions. There remains the amnesia, which is always complete for a variable period before the accident, and for the whole period of stupor and confusion, and is patchy for the terminal or Korsakow stage.

These cases of severe injury provide, as it were, a slow-motion picture of the mental disorder which follows minor injuries. In these we may see the phases of stupor, confusion, and amnesic-automatism pass in such rapid succession that the whole sequence is over in a matter of minutes. In the least severe injuries the symptoms of the earlier stages may be absent. A blow on the head may be followed immediately by automatism, without any preliminary stupor or confusion.

Many patients having recovered from the acute traumatic psychosis show residual defects—impaired memory and judgment, alteration of personality, and so on, which are very slow to recover, and remain in some cases and in some degree permanent.

The striking fact, however, is that there is no absolute correlation between the duration or degree of the traumatic psychosis and the severity of these after-effects, which I am going to call the symptoms of post-traumatic dementia. The symptoms following a traumatic amnesia of twenty-four hours, for instance, may be more severe and longer lasting than those after a traumatic amnesia of a month's duration. This discrepancy is in some cases so striking as to suggest that we may be dealing with two separate pathologies, that the traumatic psychosis may be symptomatic of some diffuse reversible molecular damage, and that the symptoms of post-traumatic dementia may be due to coarse lesions, scattered hæmorrhages, or areas of softening which are slow to resolve and may to some extent be irreparable.

Case III, to which I have already referred, affords a striking illustration of the absence of any symptoms of dementia when the patient was examined only a fortnight after the termination of an acute traumatic psychosis of six months' duration.

The following case provides an example of post-traumatic dementia in a simple setting:—

The patient, a cavalry officer, aged 40, on leave from Egypt, was found unconscious after a hunting accident on November 20, 1935. I saw him first on the 18th day after the injury when he exhibited a typical picture of traumatic confusion. From this he recovered with a traumatic amnesia of one month. Six weeks after the accident he returned home and was regarded by his relatives as normal, though his wife found him irritable. Three months after the injury, without taking any further medical advice, he returned to Egypt. Three months after this, however, his commanding officer wrote to the patient's wife stating that he had persuaded him to return home on leave as he was not fit for his work. I saw him then, for the second time, just seven months after the accident. His attitude was surly. He had been brought to see me by his wife against his will and knew nothing of his colonel's letter to her. He admitted that his work had been difficult. Formal tests showed that he could retain only six digits. Over the 100 minus 7 test he took 35 seconds with one error. I obtained his permission to write to his colonel for a report. The reply was as follows:—

"X was always a bit of a moaner, but since his injury he has been much worse. My officers who have been down to visit the detachments all said that he never stopped moaning, morning, noon and night. . . . When I first saw him he was quite impossible, would see no side of any question but his own, and was at loggerheads with the fortress commanders and staff, but he is already much better in that way. As I look at it he is a very capable and efficient officer. He is entering on another period of staff employment, and he can't afford to fall down on it as he will never get in again. . . . Is he fit to hold down this job or will it be better for his future career to let it go and wait a bit? . . . I must admit that three months ago I should have been prepared to bet that he wouldn't have lasted a month. Now I am almost persuaded that he will be O.K."

I saw him next eight and a half months after the accident. In the meantime he had been resting and playing golf. He was now courteous and amiable. Over the 100 minus 7 test he took 30 seconds with one error. He still retained only six digits. Fourteen months after the accident he performed the 100 minus 7 test in 20 seconds with one error, retained seven digits without difficulty, and reported fit for duty.

In the state of post-traumatic dementia the symptoms show a great variety, depending upon such factors as age, constitution, individual experience and environmental stress. This is in contrast with the acute traumatic psychosis in which the fundamental symptomatology shows little variation. Age is an important factor in the symptomatology of post-traumatic dementia at either extreme. In children the most prominent symptom is often behaviour disorder associated with defective moral sense. The clinical picture closely resembles that seen after encephalitis lethargica and has been well described by Strecker and Ebaugh, Beekman, and Blau. At the other extreme, impairment of the intellectual functions is usually more severe in patients over the age of 45. Constitution is perhaps the most important factor of all. There is a special liability for individuals of manic

depressive stock to an attack of this kind of illness precipitated by the injury. To this I shall refer later. Apart from this, pre-existing traits in the mood and personality tend to become exaggerated—as illustrated in the case of the cavalry officer which I have reported. Tough-minded individuals may suffer little on the side of mood or personality, tender-minded persons severely. Individual experience also plays its part. The rider-to-hounds takes concussion as an accustomed risk; the clerk is shattered by the unusual experience. Environmental stress also is important. Under any stress which is too much for them, these patients tend to become sleepless, anxious, and irritable, especially if they are constitutionally of a sensitive disposition. The cumulative stress of a compensation situation is especially likely to bring out such symptoms.

The tendency in all cases of post-traumatic dementia is towards recovery. Although this is sometimes incomplete, residual *disability* from mental disorder directly due to head injury is, I believe, extremely rare apart from coarse lesions causing dysphasia (Bonner and Taylor). I have notes only of two cases in which post-traumatic dementia has resulted in permanent disability in an adult. One was that of a man who sustained two severe injuries within the space of two and a half years. On the first occasion he was struck on the head, by a burglar, with an iron bar, with a traumatic amnesia of three weeks. He insisted on going back to his work within six weeks of the injury, but for a year was under my care with mild symptoms of post-traumatic dementia. From these he appeared to make a complete recovery, but two and a half years after the original injury he was involved in a motor-car accident and had a traumatic amnesia of two weeks. Following this, he showed a severe post-traumatic defect in the intellectual sphere. He made several attempts to get back to his work as a commercial traveller but failed, owing to his defects of grasp and memory. He became more and more depressed over his failures and, although he was awarded full compensation, he entered into a state of hypochondriacal depression and has remained a permanent invalid.

The other was a pilot in the R.A.F., who at the age of 29 had a crash, followed by an amnesia of twenty-eight days. He had subsequently made an apparent recovery and was given a ground job, but was continually getting into trouble owing to his defective memory and was eventually, after two years' trial, invalidated on this account. There were two significant points in his story. He had had a previous crash at the age of 24, with a three-day amnesia afterwards, and he had a persistent retrograde amnesia for a week before the second accident. This last point I cannot discuss fully now. My impression, however, is that a persistently long retrograde amnesia is always indicative of serious damage. The common factor in these two cases is the history of a previous injury of considerable severity. In each case functional recovery from the first injury appeared to be complete. There may, however, have been some permanent alteration of structure, and consequently less capacity for recovery after a second injury.

In children the altered disposition and behaviour disorder may persist into adult life.

All the most comprehensive studies of mental disorder following head injury have included some reference to the role played by such injury in precipitating mental illness of specific type—schizophrenia, paranoia, or manic-depressive psychosis. There are clearly two ways in which the effects of the injury may contribute towards such a development.

In the first place, as we have already observed, one of the symptoms in the state of post-traumatic dementia is an exaggeration of pre-existing traits in the mood and personality. In the second place, the injury creates a situation of invalidism and incapacity to which the patient reacts in terms of his individual make-up. These two factors, acting together, provide an opportunity for the development of schizoid, paranoid, or depressive states in individuals of corresponding disposition. Many

examples of this kind are to be found in the literature, notably those recorded by Meyer and Schilder. Illness of the manic-depressive type, however, in its major or minor degrees, may develop, in a way which suggests very strongly that it is a direct result of the organic disturbance. Schilder expresses himself clearly upon this important point; he says that

"The head injury in these cases does not act merely as a psychic trauma, but has an organic consequence for the elaboration of the psychosis."

The most convincing evidence is to be obtained from cases in which symptoms of the manic-depressive type appear before the patient has recovered from the acute traumatic psychosis, that is to say while he is still confused, and without any appreciation of the effects of his injury. I have encountered two examples of this.

(1) The first was in a man, aged 34, whose brother had an illness called neurasthenia after the Great War, and had ultimately recovered. He himself had always been a worrier and, three years before his accident, under mild stress passed through a phase of depression, with indecision and ideas of reference. In November 1934 he suffered a severe head injury followed by deep stupor, lasting three days, and subsequent confusion. While still in hospital, a month after his injury, he became depressed, thought he had cancer, and blamed himself for having given his wife their last child. Subsequently, he believed he was wanted by the police. He remained in a state of restless hypochondriacal depression. I saw him nine months after the injury in a mental hospital when he was still depressed, self-reproachful, with somewhat bizarre ideas of self-accusation, and hearing accusatory voices. He is reported to be in much the same state now, two and a half years after the injury.

(2) The second case was that of a woman, aged 49, who gave a normal family history. At the age of 22, following a broken engagement and her mother's death, she passed into a state of depression lasting several weeks, during which she was incapacitated. Else she was reported to have been active, cheerful, and capable. In August 1936 she was knocked down by a motor-cycle and had a traumatic amnesia of one week. As soon as she began to be capable of coherent conversation she begged to be taken out of hospital because she had been such a trouble to the doctors and nurses. She had heard from the other patients that in her confusion she had been difficult and this preyed upon her mind. On returning home she continued to be depressed and self-reproachful, blaming herself for her inability to sustain her domestic responsibilities. When seen, three and a half months after the accident, she was in a state of restless depression, self-reproachful and helpless.

I cannot leave this subject without some reference to traumatic neurasthenia following head injury. Why is traumatic neurasthenia, so called, more commonly encountered after head injuries than after injuries to other parts of the body? I suggest, as an answer, that the patients so labelled after head injury fall into three groups:—

(1) The group in which the situation arising out of the accident (including the compensation situation) leads to the development of hysterical or anxiety states. These are no more frequent after head injury than injury elsewhere.

(2) The group of patients who are really suffering from post-traumatic dementia. These patients are apt to react with anxiety and irritability to tasks which are beyond their capacity.

(3) The group of patients whose constitution before the accident has been of the depressive or anxious type. In this group the injury to the brain precipitates or releases an illness, which, once begun, runs its own course—usually towards complete recovery. These patients may genuinely be regarded as suffering from neurasthenia which is traumatic in a physical, rather than a psychogenic, sense.

In this brief review of a large subject I have confined myself to the common clinical effects of head injury. I have said nothing about their pathology and treatment, for I have expressed my views on these subjects elsewhere (Symonds, 1932, 1935, 1936). There are, however, one or two points about the pathology of the acute traumatic psychosis which I may be allowed to make clear. There have been attempts to

explain this in terms either of increased intracranial pressure or subarachnoid hæmorrhage. The observation of a clear, colourless spinal fluid, with a pressure of 135 mm. of water in Case III offers an example of what may be found, often enough, to discredit both these theories. I have no alternative to offer save the rather vague conception of direct molecular damage.

In conclusion there is one generalization in which I should like to indulge, however trite it may seem. The later effects of head injury can only be properly understood in the light of a full psychiatric study of the individual patient, and in particular, his constitution. In other words, it is not only the kind of injury that matters, but the kind of head.

REFERENCES

- BEEKMAN (1928), *Ann. Surg.*, **87**, 355.
 BLAU (1936), *Arch. Neurol. and Psychiat.*, **35**, 723.
 BONNER and TAYLOR (1936), *Am. J. Psychiat.*, **92**, 763.
 GOLDSTEIN (1936), *Psychiatric Quarterly*, **10**, 586.
 MEYER (1904), *Am. J. Insan.*, **60**, 374.
 PFEIFFER (1928), *Handb. des Geisteskrankheiten*. Bumke. Berlin, Springer, **3**, 415.
 RUSSELL (1935), *Lancet* (ii), 762.
 SCHILDER (1934), *Am. J. Psychiat.*, **41**, 129.
 STRECKER and EBAUGH (1924), *Arch. Neurol. and Psychiat.*, **12**, 443.
 SYMONDS (1932), *Lancet* (i), 820; (1935), *ibid.* (i), 486; (1936), *ibid.* (i), 854.

DISCUSSION

The PRESIDENT said he understood Dr. Symonds to have stated that amnesia for the period of confusion was complete even in minor cases. He himself had had a slight concussion, through falling off a horse, followed by confusion lasting about an hour. He had several apparently consecutive, but inconsequent, memories which must have gone back to a period very soon after the accident. He remembered seeing the front feet of a horse—which suggested that he was still lying down when he saw them. He then remembered sitting up and seeing a familiar landscape which he yet could not identify. Then he saw a straw stack and hated its colour; then he walked with a young man to whom he was extremely polite. All these phenomena had a dream-like quality. All were subsequently verified, but what he never remembered was that he had in fact used a great deal of bad language and been in reality far from polite. The memories were therefore selective. What might have been embarrassing to remember had been repressed. These "forgettings" did not seem to be accidental, but to depend on the ordinary laws governing repression.

Dr. THOS. TENNENT: The frequency of psychoses resulting from head injuries is generally agreed to be rare. The present study is based on 44 patients admitted to the Maudsley Hospital during the years from 1923 until 1936. I have the impression that these forms of mental illness are less rare than formerly described, and it is noteworthy that whereas during the eleven years, from 1923 until 1933, only 26 cases were admitted, during the three years, from 1934 until 1936, 18 such cases have been treated in hospital. In each of these the patient was suffering from a severe psychosis following upon an injury to the head, necessitating in each case a stay in hospital of from two to over twelve months.

Four proved to be cases of general paralysis and will not be considered further in this paper. Of the remainder, the initial symptoms were more or less the same in all, namely, confusion, varying degrees of irritability and depression, disorientation and gross memory disturbances. The clinical picture was therefore the same as that so clearly described by Dr. Symonds.

In five cases, when the degree of confusion became less marked, hallucinatory experiences and bizarre or paranoid delusional ideas became prominent. A study of the previous personality showed that each of these was reserved, seclusive, and definitely schizoid. There was evidence that two of these patients had had previous hallucinatory experiences. None of these have shown any permanent clinical improvement and four have remained in mental hospitals.

In five others the form of the illness became depressive in nature; in three of these there was a history of treatment for a similar depressive illness some years previously. Two others developed a manic reaction, part of a manic-depressive psychosis. The present state of health of these seven patients is that four have recovered from their psychosis, two are still in mental hospitals and one is dead.

Three cases occurred in children under 16 years of age. In one of these the clinical form was that of depression. The boy had been treated two years previously at the hospital during a manic phase. The form in the other two children was that of moral change. Before the accident each had been well behaved, afterwards they showed marked irritability, temper outbursts, stealing, and general intellectual deterioration. One of these has since been admitted to an institution as a moral defective; the other, according to the parents, has shown a partial improvement but remains a problem.

There remain in the series 25 patients in whom the form of illness was attributable solely to the accident. That form has been described already. In all of these patients there was marked impairment of memory. In six this was of the Korsakow type. One described vividly how Napoleon had marshalled his army the night previously, so that he, the patient, might address the men. Two, who saw active service during the war, showed an interesting ante-dating; they maintained that the war was still on and readily furnished details of their activities. All patients in this group improved and were discharged home. At the time of discharge 15 were described as "recovered"; nine as "improved". It has been possible to trace all these patients and to obtain details as to their present condition.

Of 15 discharged "recovered", 11 have maintained this state of health; two show a partial improvement—they are still employable—and two have died. Of nine "improved" at the time of discharge, seven continue in this group and two are in mental hospitals. The present state of the 25 patients in this group then, is that 11 have recovered, nine have improved, three are in mental hospitals and two are dead.

Those in the "recovered" group appear well and have no symptoms. They have required no further medical care and are able to retain employment.

Those in the "improved" group have residual symptoms. The chief of these are pains in the head, irritability, lack of power of concentration, and inability to make a decision. This inability to make a decision was quoted in practically all these cases; insight appeared to be retained, with consequent irritability on the part of the patient. Four of these patients are able to retain employment but this must be of a simple routine nature. The others are unemployable; two have developed epileptiform seizures. As might be anticipated, the presence of arteriosclerotic factors made the outlook less favourable.

These findings support the view that the prognosis for the acute psychotic symptoms is invariably good; all of these patients were discharged home. Dr. Symonds has said that permanent residual defect occurs in some cases but that this rarely amounts to disability. This is not confirmed in this series. In no less than 36% were residual symptoms found and they were of such a degree as to interfere with the patient's health and ability to earn a livelihood.

Dr. E. GUTTMANN: In co-operation with E. Winterstein I am carrying out examinations of boxers, because the "knock-out" seems to be a sort of experimental paradigm for the study of traumatic injury in general or at least of its mildest and transient forms. In order to bring some psychiatric system into the mental disorder after head injury, I adopt Jaspers' classification of the disturbances of consciousness into simple dimming, delirious clouding, and change of consciousness (as in twilight states). The disturbances observed after uncomplicated knock-outs belong to the first group, that is to say, they all show simple states between consciousness and unconsciousness and they do not show delirious features. One boxer who had a twilight state after having been knocked out, developed disseminated sclerosis later on and may have been ill already. There is sufficient reason to suppose that the transient disturbance of consciousness through knock-out is a functional one, i.e. not due to a structural brain damage. Therefore these observations seem to me a negative argument in favour of the hypothesis (brought forward by others) that a post-concussional delirium is in itself suggestive of an organic lesion of the brain. The high frequency of residual symptoms in Dr. Tennent's cases supports this opinion, since one may expect that a more detailed after-examination would have increased the number of cases with residual symptoms even beyond Dr. Tennent's 36%. Two of Dr. Symonds' cases may be interpreted in the same way, namely the two in which the patients recovered fully after simple concussion but remained damaged after a post-traumatic psychosis.

The self-observations of boxers are an interesting material with regard to the question whether the gap in the memory is a convenient measure for the duration of unconsciousness. We can time the onset of unconsciousness and we learn afterwards from our subjects how much the period between the onset of amnesia and the actual trauma varies in different

individuals. Some persons say that they felt the blow and even felt certain sensations afterwards; others saw the blow coming but did not feel it; others do not remember the whole round, the whole preceding fight, &c. Thus the retrograde amnesia enlarges the gap of memory beyond the period of unconsciousness. There may be several injuries and several retrograde amnesia, as Dr. Mapother pointed out, or there may be a subsequent confusion which should be differentiated in term and matter from unconsciousness, although both leave behind an amnesia as Dr. Tennent's cases have shown.

Dr. PURDON MARTIN said that he had been accustomed to group the symptoms and cases more than Dr. Symonds had done. There were (1) the amnesias associated with simple concussion, (2) irritative or hypomanic states which led on to a condition of confusion, disorientation, perseveration, &c., often accompanied by elation and lasting several months. These usually resulted from more severe head injuries with prolonged unconsciousness. Dr. Symonds had rejected the theory that this sequence of symptoms resulted from traumatic subarachnoid hæmorrhage, but he (Dr. Martin) still preserved an open mind on that point. He had, like Dr. Symonds, encountered cases in which the cerebrospinal fluid was clear, but unfortunately they did not often see these cases until a considerable time after the accident. In his cases in which the cerebrospinal fluid had been examined within a day or two of the accident some blood had always been present and he had never seen a case with these major mental symptoms in which cerebrospinal fluid had been normal. Examined weeks after the accident, it showed an increase in protein. (3) Thirdly, there were the late dementias. He agreed with Dr. Symonds that the prognosis in cases of post-traumatic psychosis was almost invariably good, but he had seen two or three cases in which, about a year after the accident, when a great degree of recovery had occurred, the patients had relapsed and progressively deteriorated. In one instance, the patient, a railwayman, had become well enough to go back to partial work for a time before relapsing. (4) The fourth group was formed by "traumatic neurasthenia", and he was grateful to Dr. Symonds for his analysis of this group. He strongly supported the view that some cases classed as traumatic neurasthenia were really mild cases of traumatic psychosis or dementia and had some organic basis.

He wished to make particular reference to the symptom of elation. He believed that it had some localizing significance and indicated an injury of a frontal lobe. It was related to "Witzelsucht". It was now beginning to be seen as a result of operations involving removal (or partial removal) of a frontal lobe. In his experience, when it occurred after a head injury it persisted throughout the patient's illness and one of its effects was to prevent the occurrence of an anxiety state.

Section of Neurology

President—C. M. HINDS HOWELL, M.D.

[April 22, 1937]

Localized Symmetrical Cortical Sclerosis in an Infant.—RUBY O. STERN, M.D. (by permission of Dr. W. J. PEARSON).

Clinical history.—Fred. T., six months old, a twin, admitted to the Hospital for Sick Children, Great Ormond Street, April 26, 1935, under the care of Dr. W. J. Pearson, on account of "screaming attacks and rigidity of the spine". He had had these attacks at night and after each feed for three months, but for six weeks the screaming had been almost continuous. No vomiting or diarrhoea.

On examination.—Well-nourished infant lying in a position of opisthotonus. Fontanelle not tense. Nothing abnormal found in abdomen, heart, or lungs.

Cranial nerves: Discs reported to show primary optic atrophy. Otherwise cranial nerves normal. *Arms:* Power good; arm-jerks present and equal. *Legs:* Power good; knee- and ankle-jerks present and equal. Plantars equivocal. Kernig's sign present. Abdominal reflexes not obtained. Response to pin-prick normal. Sensation could not otherwise be tested.

Investigations.—Cerebrospinal fluid normal; ventricular fluid normal. Skiagram of skull normal. Mantoux reaction negative.

Ten days after admission head retraction became worse and was not lessened by repeated lumbar puncture. The infant lost weight rapidly, vomited frequently, and died four days later.

(History subsequently obtained from mother: The twins were born by normal labour at the seventh month. The surviving twin, also a boy, has remained quite healthy up to the present time.)

Post-mortem examination.—The brain weighed 530 grm. At the tip of each occipital pole there was a firm, white, wrinkled area, slightly raised above the surface of the surrounding brain tissue, as if inserted into it. This area measured about $1\frac{1}{4}$ cm. by 1 cm. at the occipital poles, but it extended on each side into the calcarine fissure for a distance of about $2\frac{1}{2}$ cm. as a narrow band, about $\frac{1}{2}$ cm. in width. No similar areas of sclerosis were found elsewhere in the brain and no congenital or other abnormalities were found elsewhere in the body.

Microscopical examination.—It was unfortunate that neither the optic nerves nor the anterior portion of the optic chiasma were available for microscopy. The remaining portion of the chiasma, the thalamus, basal ganglia, and optic tracts were sectioned, but nothing abnormal could be detected. Sections from one of the sclerotic areas showed complete replacement of nerve-cells and nerve-fibres in the cortex and subjacent white matter by a dense mass of neuroglial fibres which stained well with Anderson's Victoria blue stain. There was a sharp edge to this area and beyond this edge the tissues stained normally. The blood-vessels appeared healthy and there was no evidence of an existing or previous inflammatory process. In the absence of a vascular lesion, a history of birth injury, or evidence of pre-existing inflammation, there would appear no alternative but to regard the condition as a congenital gliosis of unknown aetiology.

Tumour of the Optic Nerve, Chiasma, and Thalamus.—RUBY O. STERN, M.D. (by permission of Dr. DONALD PATERSON).

Clinical history.—Joan E., aged 3 years and 10 months, admitted to the Hospital for Sick Children, Great Ormond Street, June 8, 1936, on account of weakness of legs and unsteadiness in walking (duration three months), and incontinence of urine (duration six months).

On examination.—Pale, well-nourished child, slightly dull mentally, not always understanding what was said to her, though she tried to co-operate in the examination. Small café-au-lait patches were scattered over the trunk and limbs.

Cranial nerves: Both discs showed considerable papilloedema, more on right side than on left. Slight weakness of the right facial muscles; otherwise cranial nerves normal. *Arms:* Slight weakness and dubious spasticity. *Arm-jerks* normal. *Legs:* Muscular power diminished on both sides. Slight spasticity of left leg. *Knee-jerks* brisk, left > right; *ankle-jerks* brisk, left > right. *Plantars* both flexor. *Gait* ataxic with a tendency to fall backwards.

Sensation normal—as far as could be ascertained.

Cerebrospinal fluid normal. Skiagrams of skull in usual positions showed no abnormalities.

A mid-line cerebellar tumour was suspected and Mr. C. Donald performed a sub-occipital decompression and explored the cerebellum. No tumour was found, but the pressure of the cerebrospinal fluid was much raised. The child died twelve days after operation. No further neurological signs developed before death.

Post-mortem examination.—The right optic nerve was diffusely enlarged from the eyeball to the chiasma, the greatest enlargement being towards the chiasma, whilst the chiasma itself was thickened to nearly twice its normal size. On dissection of the brain after fixation the right optic thalamus was found to be enlarged and consisting mainly of white tumour substance, distinguishable with difficulty from the white matter of the thalamus, until palpated, when its firm consistency revealed its nature.

Microscopical examination.—The tumour was composed of oval and spindle-shaped cells with very little cytoplasm, arranged in strands, with their long axes roughly parallel. The nuclear chromatin was well defined; no mitotic figures were seen. No neuroglial fibres could be demonstrated either by the Victoria blue stain or by Mallory's phosphotungstic acid method, but in sections stained by the latter method a process could be seen arising from either end of many of the spindle cells. These processes varied in length, and though usually straight, occasionally presented a corkscrew-like appearance. There was little connective tissue present in the tumour except around the blood-vessels which were fairly numerous and thick-walled.

The histological appearances of the tumour suggested that it should be classed as a spongioblastoma polare, as it conformed closely to the description of that tumour of the optic nerve given by Bailey and Eisenhardt (1932, *J. Comp. Neurol.*, 56, 391).

Polioencephalitis Hæmorrhagica Superior.—J. St. C. ELKINGTON, F.R.C.P.

Mrs. D. R., aged 56.

Family history.—Negative. Husband alive and well. Two healthy grown-up children. No children dead, and no miscarriages.

Past history.—Had worn a belt for twenty years for "floating kidney." In 1923 had an operation for piles and a fistula. First attended the out-patient department in July 1934, complaining of abdominal discomfort and scalding micturition. This cleared up with symptomatic treatment, but from August 1934 until June 1936 she attended the out-patient department regularly on account of flatulence and discomfort after food. She returned again on August 8, 1936 complaining of difficulty in thinking and pains in her legs of fourteen days' duration.

On examination.—Loss of memory for recent events. Pupils sluggish in reaction to light, but in other respects cranial nerves were normal. Knee- and ankle-jerks absent; muscles of legs hypotonic; plantar responses flexor. Patchy loss of sensibility to pin-prick in both legs, and vibration-sense diminished in both malleoli. No anaemia. Tongue normal.

Attended out-patient department again next day when, in addition to the above signs, it was noted that the discs were normal. There was slight nystagmus on deviation to right and left, and blood-pressure was 150/90.

September 18, 1936: Admitted to St. Thomas's Hospital, under the care of Sir Maurice Cassidy.

On admission.—The patient's mental state was such that she could give no reliable history, but she still complained of pain in legs, difficulty in walking, and loss of memory. Her daughter said that for about a year walking had produced pain in both legs, and for the last month this pain had been practically continuous. For a month the memory and power of concentration had steadily diminished, and there had been a tendency to depression and emotional outbursts. She had not complained of headache, but had felt muddled in her head. There were no other symptoms. No history of alcoholic indulgence could be obtained from the patient or relatives.

On examination the patient was drowsy, but could be roused. She was disorientated in all spheres, and memory for both remote and recent events was poor. Attention could only be maintained for a short time. Speech was slightly hesitant and spaced, suggesting mild cerebellar dysarthria. No aphasia. Fundi and visual fields were normal. Visual acuity: $\frac{6}{24}$, right; $\frac{6}{36}$, left. Bilateral ptosis. Pupils were slightly irregular in outline; reacted very sluggishly to light but better on attempted convergence. Conjugate upward deviation of the eyes absent; conjugate deviation to the right absent, but movement to left and downwards was full. Convergence not possible. Rotatory nystagmus present in all directions of gaze. Slight weakness of left side of face, but in other respects cranial nerve functions normal. Limbs hypotonic and generally wasted. Muscles of both calves distinctly tender to pressure; muscular strength everywhere less than normal. Outstretched hands were slightly tremulous; definite intention tremor in both arms, especially left. Tendon reflexes lost throughout; the abdominal reflexes were absent, and the plantar responses flexor. As far as could be ascertained there was diminution of sensibility to pain and light touch below knees and elbows.

Examination of the other organs was negative. The liver could not be felt. The heart was normal for her age; the blood-pressure was 125/80. The urine contained a slight trace of albumin.

Investigations

Cerebrospinal fluid.—Initial pressure 55 mm.; no evidence of subarachnoid block; two cells per c.mm. Total protein 0.02%. Lange normal. Wassermann reaction negative.

Blood.—Wassermann and Sachs Georgi reactions negative.

X-ray examination of chest, negative.

Test meal.—Before histamine: volume 42 c.c. After histamine: volume 20 c.c. Odour slightly sour; bile absent; blood traces; food residues + + +; free hydrochloric acid absent; lactic acid + + +.

After admission the patient's condition steadily declined without the appearance of any very definite signs. The temperature began to rise seven days after admission, and on the tenth day she died with a temperature of 108° F.

Report of Post-mortem Examination of Brain

Macroscopical appearances.—The brain on removal appeared to be normal except where the medulla was cut across, and here the grey matter appeared more congested



FIG. 1.—Hæmorrhages into peri-aqueductal grey matter.

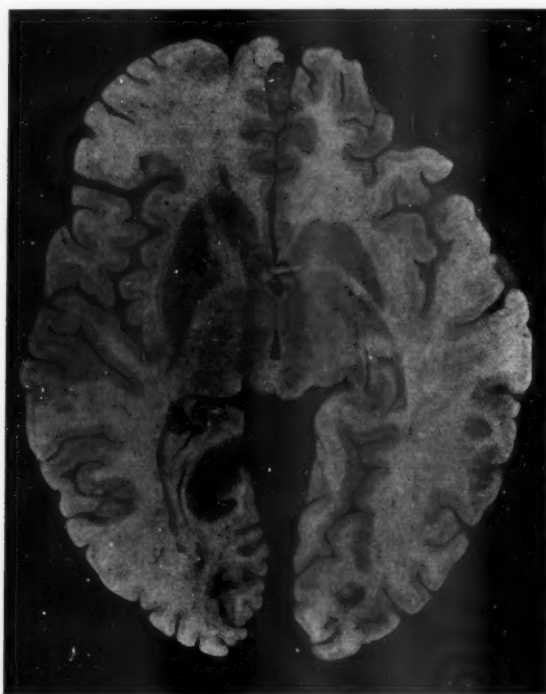


FIG. 2.—Hæmorrhages into peri-ventricular grey matter.

than normal. The brain was hardened. Afterwards the brain stem was divided through the cerebral peduncles when it was obvious that the grey matter around the aqueduct of sylvius was abnormal. For an area about $\frac{1}{2}$ cm. in radius it was grey in colour, with numerous punctate hæmorrhages. The abnormal area was very strikingly demarcated from the surrounding tissue. The hemispheres were divided by horizontal sections from the vertex downwards. Everything appeared normal until the section passing through the 3rd ventricle, when it could be seen that the medial aspects of both thalami immediately under the ependyma of the 3rd ventricle were congested and contained small hæmorrhages.

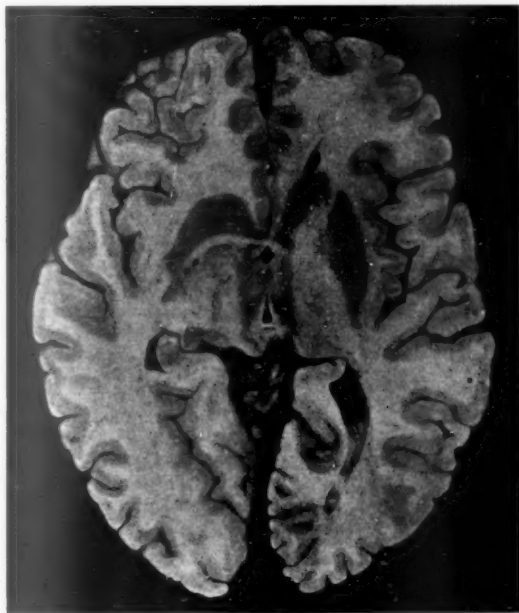


FIG. 3.—Hæmorrhages into peri-ventricular grey matter.

In the next section passing through the anterior, middle, and posterior commissures and through the superior corpora quadrigemina, a zone of hæmorrhagic encephalitis could be seen extending for a distance of $\frac{1}{2}$ cm. or so from the ventricular cavity.

Serial sections through the mid-brain, pons, and medulla showed that the alteration in peri-aqueductal grey matter extended caudally as far as the 4th ventricle where it gradually disappeared. The medulla and pons, as far as could be seen macroscopically, were normal.

Microscopical appearances.—The pathological changes were confined to the peri-ventricular and peri-aqueductal grey matter. The outstanding feature was the presence of a large number of hæmorrhages of different size containing recently shed blood. Most of these were round small blood-vessels, and in places one could see the disrupted endothelium of the capillaries. In others of the hæmorrhages no direct relationship with the capillaries could be seen. Although these hæmorrhages for the most part appeared to be quite recent, some of them showed considerable

quantities of old blood pigment. The blood-vessels, other than those showing hæmorrhage, appeared normal. The surrounding brain tissue was normal except for moderate increase in number and size of the neuroglia nuclei and there was no perivascular cuffing.

Jakob's Syndrome (Senile Dementia with Parkinsonism).—MACDONALD CRITCHLEY, M.D., F.R.C.P., and J. G. GREENFIELD, M.D., F.R.C.P.

In 1923 Jakob described a case of senile dementia associated with Parkinsonism, and distinguished this condition from arteriosclerotic dementia, which it resembled closely in its clinical features, but not in its pathology. There was no disease of the cerebral vessels, but the senile plaques and fibrillary changes in the nerve-cells, found in senile dementia, were combined with the lesions in the basal ganglia and substantia nigra found in paralysis agitans. A few similar cases have been described but the condition appears to be rare.

The present case is that of a Belgian woman, aged 64, who was admitted to the National Hospital, Queen Square, on March 11, 1936, and died eighteen days later.

History.—Mental deterioration for two years; stiffness of limbs and tremor in hands, jaw, and tongue for one and a half years. Speech had gradually become more mumbling and indistinct; for the past year had been a continuous incoherent jabber. On examination she was restless and inco-operative, jabbering incessantly and monotonously; speech quite meaningless. Face mask-like; fine rhythmical tremor of lower jaw and trumbone tremor of tongue. Ocular movements normal, with the exception that convergence was impossible. Arms held in a Parkinsonian attitude: intermittent tremor in right hand and arm. Gait typical: tendon-jerks present without exaggeration; abdominal reflexes absent; right plantar reflex flexor; left, doubtfully extensor, in type.

Post-mortem examination of the brain showed the convolutions to be generally somewhat shrunken, but there was no thickening of the pia-arachnoid and the arteries at the base were healthy. On section of the mid-brain the substantia nigra was found to be rather pale, and the area occupied by it rather wider than normal.

Microscopical examination showed a degree of lipid infiltration of the nerve-cells in all areas, rather greater than normal for the patient's age. There were also, in the cortex of the frontal, Rolandic, and hippocampal regions, numerous senile plaques of varying size, but no cells showing Alzheimer's fibrillary change could be seen. A few of the Betz cells, however, showed Nissl's chronic degenerative changes. There was a slight thickening of the processes of the cortical astrocytes but there were very few swollen neuroglial fibres. In the basal ganglia the most striking abnormality was the presence, in the globus pallidus only, of large droplets of lipid, chiefly isotropic but containing small anisotropic granules. These globules appeared to be chiefly extracellular. There was no evident loss of nerve-cells in the basal ganglia and no abnormal forms of neuroglia were seen in them. In the substantia nigra there was a considerable loss of cells, and numerous granules of melanin could be seen lying free in the tissues or collected round the vessels. This change was not of so severe a degree as is common in post-encephalitic Parkinsonism but it was quite marked. There was no evident difference between the substantia nigra on the two sides. Except for slight perivascular infiltrations the pons was normal. The medulla was healthy as was also the cerebellum, apart from an occasional "torpedo" on the axons of the Purkinje cells in the granular layer.

The microscopical picture therefore, like the clinical picture, was that of a combination of senile dementia with paralysis agitans. But the onset of these two

conditions within a few months of one another suggests that this was more than a chance association. It is true that both are diseases of the senium and it is possible that a rapid onset of senility might have precipitated both conditions at about the same time. Whether Jakob's syndrome should be regarded as a separate morbid condition, or as the association of two diseases, has been discussed recently by Grünthal, who is inclined to the latter conception, since the pathological pictures of senile dementia and paralysis agitans are ill-defined, and lesions both of the cortex and basal ganglia may be found in cases in which the symptoms are predominantly those of one or other disease. Morbid process of senility severely implicating the palato-striatum is, however, a striking clinico-anatomical phenomenon, and for this reason it is convenient to isolate this syndrome under the term Jakob's disease.

Spontaneous Hæmatomyelia: a Report of Two Cases, one in Association with an Intramedullary Angioma, and the other in Association with Syphilis.

—J. CLIFFORD RICHARDSON, M.R.C.P.

The following two cases illustrate the clinical features of hæmatomyelia, and the early and late reactions of the spinal cord tissues to hæmorrhage, as well as indicating two interesting causes of the condition.

Case I.—A man aged 25, patient in the National Hospital, under the care of Dr. Hinds Howell.

Clinical history.—He was well until seven weeks before admission, at which time he noticed a numbness of the sole of his right foot. This spread slowly over the foot and up the back of the leg to the knee: at the same time he suffered constant severe pain across the back in the lumbar region. Four weeks after the onset his right leg became slightly weak. Five weeks from the onset, after playing a strenuous game of football, he had severe pain and stiffness of the back and legs. In the subsequent two days the pain was very severe, and there was a rapid development of complete loss of power and feeling in the legs, with retention of urine and fæces. He was admitted to hospital a fortnight later in this same condition.

Clinical examination.—Cranial nerves and arms normal. Lower abdominal muscles weak; legs flaccid and completely powerless. Tendon reflexes normal in arms, absent in legs. Right upper abdominal reflex weak, right lower absent; both left abdominal reflexes normal. All forms of sensation were absent below a level at D.12 right and L.1 left. A band of hypo-algesia was present from D.5 to D.9 on the right, with an intervening band of hyperalgesia.

The urine contained many pus cells. The cerebrospinal fluid was normal except for a raised protein content of 0.090%, and there was no evidence of a block on jugular compression. Wassermann reaction negative in cerebrospinal fluid and blood. Temperature was normal on admission. No leucocytosis or anaemia. Clinical diagnosis: subacute myelitis.

The patient became progressively worse, from an intractable infection of the urinary tract, and died of acute suppurative pyelonephritis, and gangrenous cystitis, thirteen weeks after the onset of symptoms.

Post-mortem examination.—At autopsy the spinal cord looked normal except for a slight diffuse swelling of the lumbar enlargement, and rather large pial vessels in that region. Section of the cord showed a rounded cavity containing old blood, running down from the lower border of the 4th dorsal segment to the lower end of the cord. Above, the cavity was small and situated in the right posterior horn. At the 9th dorsal segment it became more median, lying between grey and white matter, and at the 12th dorsal segment it became larger and crossed the mid-line.

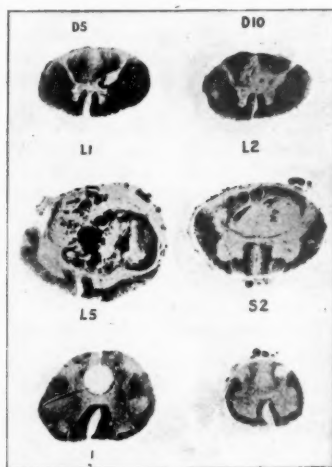


FIG. 1.—*Case I.* Sections of spinal cord at various levels, showing the position of the hæmorrhage. The angioma is seen in the posterior column at L.1. ($\times 2.2$) Loyez stain.

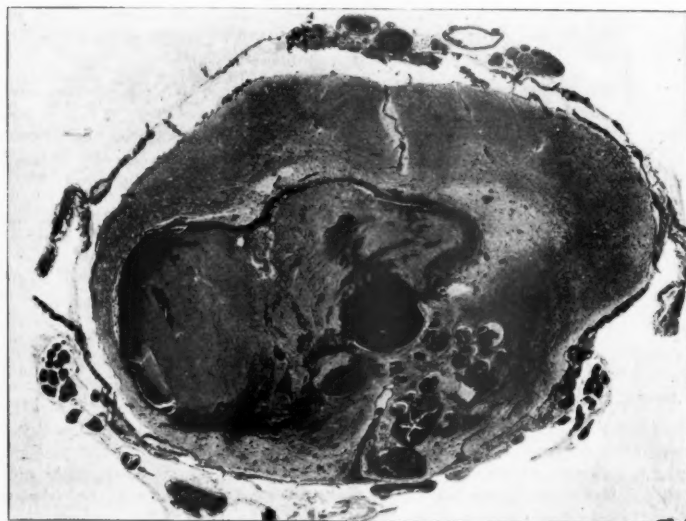


FIG. 2.—*Case I.* Section through the angioma, showing a ruptured vessel and the adjoining large hæmorrhage. ($\times 36$.) Hæmatoxylin and Van Gieson.

The hæmorrhage was largest at the first lumbar segment, and below this ran down as a central cavity in the posterior columns, to the lowest segment of the cord. The physical signs coincided fairly accurately with this position of the hæmorrhage.

On the posterior part of the section through the area of largest hæmorrhage there was a small, oval, yellowish, porous-looking area of abnormal tissue. Microscopically this was found to be a small angioma confined to that segment. It consisted of a localized collection of large and small thin-walled blood sinuses. In a few the structure resembled normal veins, but they were mostly poorly formed, consisting of a thin layer of collagen with a single lining layer of endothelium. There were some localized hyaline thickenings of the walls. The tissue between these sinuses was hæmorrhagic and composed of glial tissue, condensed in some areas with scattered bands of connective tissue, and some nerve-fibres. An actual point of rupture of one of the larger sinuses was seen in some sections.

The clinical symptoms suggest that a slow leakage occurred at first, then a more massive hæmorrhage. This severe hæmorrhage, following a game of football, was probably provoked by the spinal venous congestion subsequent to strenuous exertion.

The hæmorrhage appeared fairly recent, being composed of intact red blood-cells, with a relatively small amount of blood pigment at the periphery. It appeared oldest in the 1st and 2nd sacral segments, which corresponded with the earliest symptoms of numbness in the foot and back of the leg.

The white matter at the margin of the hæmorrhage was severely degenerated. There was some perivascular infiltration of lymphocytes, and some proliferation of capillaries. In the grey matter of both anterior and posterior horns there were pronounced degenerative changes in the nerve-cells, with neuronophagia, and disappearance of cells.

Vascular tumours and malformations of the spinal cord are decidedly rare, but in the few cases reported, hæmatomyelia is a not uncommon complication. The angioma in this case is probably a congenital maldevelopment primarily, and is perhaps more correctly termed a hamartoma than a tumour. Very similar tumours with hæmatomyelia have been reported by Lissowsky, Buckley, and Ohlmacher.

Case II.—A man aged 58, patient in the National Hospital, under the care of Dr. Kinnier Wilson.

Clinical history.—Seventeen months before admission, he was suddenly awakened at night by severe pain across the lower abdomen. There was a rapidly increasing weakness of the legs in the next two days. Twenty-four hours after the onset he had a numb patch over the upper part of the front of his right thigh. After two days the legs, bladder, and bowel were completely paralysed, and he had a numb, dead feeling up to the waist. The pain had disappeared by the time this final picture had presented itself. In St. Mary's Hospital soon after the onset, an examination of the cerebrospinal fluid showed a strongly positive Wassermann reaction, 15 lymphocytes per c.mm., a raised globulin content, and a meningitic gold curve. The blood Wassermann reaction was also positive and antisyphilitic treatment was given.

He remained in the same state for one month, then gradually recovered. Power slowly returned in both legs but at the same time he had a constant tight painful feeling in both legs and about the hips, and had frequent painful flexor spasms of the legs. One year after the first attack he began to suffer much more severe pain in the legs, and this brought him to hospital.

Clinical examination.—The pupils reacted a little sluggishly to light, otherwise the cranial nerves were normal. There was a spastic paraplegia, the right leg being worse than the left. Slight wasting of right glutei, hamstrings, and quadriceps.

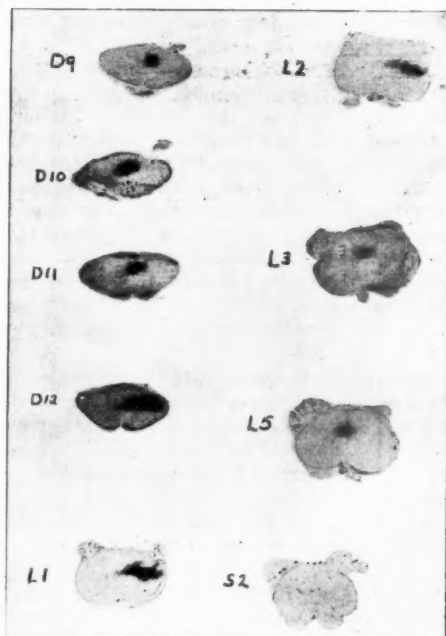


FIG. 3.—*Case II.* Sections of spinal cord at levels from D.9 to L.5, stained for iron to show the position of the old hæmorrhage. ($\times 1.7$.)

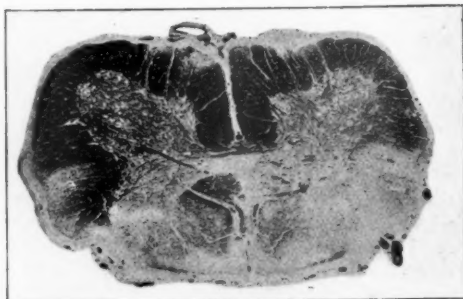


FIG. 4.—*Case II.* Second lumbar segment. Pale area of myelin destruction in the right posterior column, posterior horn and lateral column. This is the maximum area of blood pigmentation and gliosis. Descending degeneration in pyramidal tracts. ($\times 8$.) Loyez stain.

Vibration sense was lost in both legs. Position sense was grossly impaired in the feet; worse in the right foot. Light touch was slightly impaired over the legs below the knees, otherwise there was no loss of cutaneous sensation, and there was no sensory level on the trunk. Gait very spastic. Cerebrospinal fluid examination was now entirely negative.

The patient became progressively worse and died from an intervening infection of bladder and bowel, twenty months after the onset of symptoms.

Post-mortem examination.—There was slight thickening and adhesion of the meninges over the dorsal surface of the cord, and very slight softening at D.12. Section of the cord showed the brown scar of an old hæmatomyelia, extending from the 9th dorsal to the 4th lumbar segments. The pigmented area stained deeply by the Prussian blue reaction for iron. Above, the area of old hæmorrhage was small and rounded, lying just behind the posterior commissure. It became larger as it ran down and showed a lateral extension to the right cord margin in the 12th dorsal and 1st and 2nd lumbar segments, thus involving the posterior column, base of posterior horn, and lateral column. At L.1 it also invaded the base of the anterior horn. In the 3rd and 4th lumbar segments the hæmorrhage was again small and tubular, confined to the right posterior column.

Microscopically there was no cavity, nor were there any free red blood-cells. There was a heavy deposit of blood pigment, mostly contained in macrophages forming thick cuffs around the vessels in the posterior columns. Several lymphocytes were scattered amongst the pigment-laden phagocytes. In some areas the small vessels were surrounded by a pure round-cell infiltration and, in other places, the whole thickness of the vessel was infiltrated by lymphocytes. A localized inflammatory reaction of this type was seen in one large pial vein. This reaction, occurring distinct from the perivascular cuffing by macrophages containing iron pigment, was the most definite evidence of syphilitic vascular disease that was found. The exact source of hæmorrhage was not detected. Possibly rupture had occurred in one of these small syphilitic vessels.

A dense glial scar was present in the area of pigmentation, most pronounced centrally, with a lateral projection through the posterior horn to the lateral column in some areas. Large astrocytes with heavy neuroglial fibres were seen by phosphotungstic acid hæmatoxylin stain. There was also pronounced marginal gliosis with tufts spreading out into a thickened pia.

Pronounced local destruction of myelin and nerve-fibres was shown by Loyez stain as pale areas in the region of pigmentation and scarring. There was also a well-defined ascending degeneration in the posterior columns and descending degeneration in the pyramidal tracts.

This long tubular and flattened strip of blood pigment is probably the relic of an extensive hæmorrhage. Its distribution is similar to that of the first case, though probably the hæmorrhage was smaller. The history of onset and the persistent pain support the contention that the lesion was primarily a hæmatomyelia. The hæmorrhage cavity had been entirely filled in by a glial scar. The whole pathological picture is one of hæmorrhage rather than of softening.

There have been a few scattered reports of syphilis as a cause of hæmatomyelia—though it would seem distinctly uncommon.

The tendency for hæmatomyelia to spread out in the grey matter, particularly in the posterior horn, has been amply shown by reported cases, and experimentally by injections of blood and dyes into the spinal cord (Goldscheider and Flatau, Lépine). It is explained by the greater vascularity and softer texture there.

Pain was a striking feature of these two cases. In both severe pain was the first symptom, and in the first case pain was distressing throughout the illness. This was

probably due to irritation of the posterior horn cells by extravasated blood. In the second case it was of interest that the pain stopped and then recurred very severely one year later—suggesting some relation to the forming of a glial scar in the posterior horns.

REFERENCES

- LISSOWSKY, P. (1931), *Ztschr. f. d. ges. Neurol. u. Psychiat.*, **148**, 691.
BUCKLEY, A. C. (1936), *J. Nerv. and Ment. Dis.*, **83**, 422.
OHLMACHER, A. P. (1849), *J. Nerv. and Ment. Dis.*, **26**, 395.
LÉPINF, JEAN (1900), *Thèse de Lyon*.
GOLDSCHIEDER und FLATAU (1897), *Ztschr. f. klin. Med.*, **31**, 175.

United Services Section

President—Surgeon Rear-Admiral J. FALCONER HALL, C.M.G.

[April 12, 1937]

A Clinical Note on Fungus Infection of the Skin of the Feet

[ABBREVIATED]

By Surgeon Commander J. C. SOUTER, R.N.

DURING the last twenty years increasing interest has been taken in the subject of fungus infection of the skin of the feet. The disease is of peculiar interest to the Services because, though in most cases no symptoms at all, or only discomfort due to itching, may be experienced, yet every sufferer is a potential casualty, owing to the possibility of an acute exacerbation necessitating treatment in bed. In addition, irritable or painful feet try the temper and induce fatigue in those who have to march distances in heavy boots (Jones, 1935).

Many names are given to the disease—such as Hongkong, Shanghai, and Singapore foot, athlete's foot, "gym," golfers' and swimmers' itch, toe-rot, ringworm of the feet, Cantlie's foot tetter, eczematoid ringworm of the extremities, dermatomycosis, epidermomycosis, and epidermophytosis. Whitfield described ringworm of the toes in 1908. Since the Great War it has become more common, and it may be that the service of men of many nations in tropical and subtropical countries, with resultant infection and return home uncured, tended to spread the disease (Hallows, 1922; Barksdale, 1933). It is now of world-wide incidence and is becoming relatively and actually more prevalent (Jamieson and McCrea, 1932; Strickler and Friedman, 1931). Student bodies show a high incidence (Hulsey and Jordan, 1925; Sharp and Taylor 1928; Legge *et al.*, 1929; Gould, 1931), and students from India, China, Japan, &c., may have played a part in the spread. It is also common among the general population (Semon, 1934; J. Witton Flynn, 1935; Buchbinder, 1934; Cumming, 1928), with the higher strata of society showing more cases (White, 1927); the hospital class of patient is also affected (Muskatblit, 1933). I have recently examined the toes of various groups of candidates for entry into the Royal Navy and, though no definite diagnosis of epidermophytosis could be made, it was surprising to find how many showed scaling, maceration or fissuring between the toes. The percentage incidence was:—

Group	Age	Percentage affected
Recruits from working-class homes ...	16-18	2.4
Public school boys ...	17-18	41.0
Preparatory school boys ...	13	5.9
Bankers, schoolmasters, &c. ...	22-28	50.5
Mercantile marine officers ...	21-29	67.2

In several groups of officers and men, comprising over 3,000, the number showing clinical evidence of fungus infections of the skin of the feet varied from 26.6% at home to 42.6% on the China Station. When officers alone were considered, this percentage rose to 44.2 and 63.4%. Various groups of ratings showed no appreciable variation of incidence. A series of 500 officers and men in the United States Navy showed an incidence of 13.2%. 90.9% of the officers were affected (Butler *et al.*, 1924).

The disease is rare in young children, in contradiction to the frequency of ringworm infections of the scalp (Graham-Little, 1916). The age-groups from 20 to 40 years show the highest incidence (White, 1927; Williams, 1936), while men are more susceptible than women (Strickler and Friedman, 1931). Many patients have had the

disease for years before reporting for treatment (White, 1927; Ormsby and Mitchell, 1916).

The disease is commoner among those who are gathered together in communities like public schools, ships, &c., where bathing is frequent and communal. Among the general population it is rarer in the poorer classes of society where opportunities for bathing are scanty.

I do not propose to discuss the various fungi which are of pathogenic importance in epidermophytosis. Trichophyta and epidermophyta are most commonly found. They may be present on normal skin surfaces (Williams, 1922; Cornbleet, 1926), and in such cases may be saprophytic, setting up dermatoses only when conditions are favourable for growth. The fungi have both a corrosive and irritant action by the elimination of a keratolytic, toxic ferment, and their own rapid growth (MacLeod, 1928). Mycelium has been shown by biopsy as far down as the tenth layer of epidermal cells (Jamieson and McCrea, 1932). Fungi grow rapidly on hair, wool, silk, &c., and on algal growths from damp floors, and remain viable after long periods of drying (Bonar and Dreyer, 1922).

A diagnosis can be made on clinical grounds alone (Guy and Jacob, 1923), but in doubtful cases it is well to look for the fungus. The species can be identified only by cultural methods (Muende, 1934). Various methods are described for examining for fungi microscopically (Roxburgh, 1934; Jones, 1935; Swartz, 1936; Morris Moore, 1936; Milochévitch, 1936). The so-called "mosaic fungus", crystals, oil and fat globules and degenerate cells must be differentiated, and it is necessary to make sure that there are no imperfections on the cover-glass.

The disease is more common in hot countries and particularly so in climates and during seasons with a high relative humidity. Heat and moisture are necessary for favourable growth of the fungi. Excessive sweating is an accepted predisposing cause of epidermophytosis (Weidman, 1928), and McCormick (1935) has emphasized how tight-fitting, badly fitting, modern shoes produce ideal conditions for fungus growth, particularly if an orthopaedic abnormality such as flatfoot is present (Cornbleet, 1934). The sweat in intertriginous areas is highly alkaline, and treatment of fungus skin lesions by acids has been suggested (Marchionini, 1929, 1930; Levin and Silvers, 1932; Maschkilleisson *et al.*, 1934; Belisario, 1935).

Re-infection by organisms harboured in shoes has been investigated, and many patients gave a history of irregular recurrences irrespective of whether old or new shoes were worn (Jamieson and McCrea, 1937).

The dhobi or washerman has been blamed for the spread of the disease. I have never seen a case of clinical epidermophytosis in a Chinese of the coolie class accustomed to walk barefoot or wear pattens, and to this class the washerman belongs. On the other hand, the disease is common in westernized Chinese who wear shoes. The fault lies in imperfect laundering and, especially, imperfect drying, of socks; it is not that the washerman is himself infected.

Cases have been recorded of familial infection (Lovejoy, 1923) but this is not common, and men rarely infect their wives—women being extremely insusceptible. They wear thin stockings and light, well-ventilated shoes, and take more interest in the hygiene of their feet than men do. Apparently infection is not spread from patient to patient but an inanimate object intervenes (White, 1927). Towels, wooden gratings in bathrooms, coconut matting, and wet floors and decks in swimming baths, &c., are potential sources of spread. It is surmised that trauma, however slight, is necessary for the fungus to gain an entrance, and this may be effected by particles of sand, the action of caustics on bare feet in cleaning decks, the "rubbing" of a clumsy darn in a sock or an abrasion from a badly fitting shoe. Many patients report exacerbations after bathing in the sea. Wading spreads the toes and aggravates fissures (Skeoch, 1928).

To contract the disease, heat, moisture, and a trauma are required, with contact

with an object on which the fungus is present. I believe that epidermophytosis of the feet is common in those members of the community who bathe often, not because the skin surface is in any way changed by frequent washing, but because it is so often left imperfectly dried.

Descriptions of the clinical appearances of epidermophytosis are to be found in the standard textbooks on dermatology and elsewhere. White (1927) describes 11 different types. For present purposes I propose to discuss briefly three main groups, intertriginous, hyperkeratotic, and vesiculo-bullous, the first two running a chronic course with acute exacerbations, and the third showing, usually, an acute onset and often passing into a subacute or chronic stage, also with exacerbations. The intertriginous type is most common and Weidman (1927) believes that it represents the primary lesion in all cases. One or both feet may be affected and one or more of the interdigital clefts may be involved, with the original infection in a fourth cleft in every case. The predilection of the fungus for this particular cleft has aroused interest and has been explained on anatomical grounds (Gray, 1927; White, 1927). The little toe is often squeezed out of its normal shape by the shoes and liable to be abraded. But this does not occur in all cases and Weidman (1927) thinks further investigation is required. There may be simply scaliness in the clefts but usually the skin in the space is macerated and shows a dead-white, sodden, thickened, adherent mass of epithelium (Ormsby, 1935), like moist blotting paper or suede leather (Macleod, 1928). Sodden pearly plaques are sometimes seen (Jones, 1935) or the epithelium may become thickened at one place to form a "soft corn" (Gray, 1934). No symptoms may be experienced until an exacerbation occurs (Hallam, 1928). The epithelium peels off leaving a red, painful area on which vesicles may form and spread on to the plantar or dorsal surfaces of the toes or of the foot itself (Franklin, 1935). Fissures form vertically across the webs, or laterally at the junction of the toes and the ball of the foot, and cause discomfort and even pain, and may prevent the patient from walking.

Hyperkeratosis of the soles and heels, and in the region of the ankle, happens as a result of long-standing vesicle formation in thickened epidermis (Franklin, 1935), and may appear as irregular patches with detached edges (Macleod, 1928) or as round keratoses, the size of a split pea, either projecting above the surface or lying imbedded in the horny layer (White, 1927). The keratotic areas are coloured yellow or brownish yellow, and are not painful unless fissures form. Secondary infection may take place and the whole of the skin of the foot become sodden and exude foul-smelling sanguineous sero-pus.

Vesicles and bullæ arise either as a direct spread from the interdigital clefts or on the dorsum of the toes, dorsum and sole of the foot, &c. The vesicles are arranged in clusters (Scholtz, 1932) and are deep-seated or superficial, and varying in size. They do not appear simultaneously and are not necessarily symmetrical. Unless secondarily infected the contents are clear but often show surrounding erythema. The clusters spread from the periphery (Scholtz, 1932) either in all directions or from one point only (Ormsby, 1935). Itching is invariable and can be relieved by rubbing or scratching (Barksdale, 1933).

The vesicles may dry up, or be ruptured by scratching and an erythematous, scaly patch be left, often with a defined edge, and fresh vesicles may form on the patch or at its edge. In other cases the rupture of the vesicles may leave behind a red, shiny, or weeping surface surrounded by a collar of scales (Ormsby, 1935). Sometimes the vesicles may run together to form bullæ, and with secondary infection the whole foot may become inflamed and swollen, with cellulitis, lymphangitis, enlarged and tender groin glands, fever and constitutional disturbance. Such acute manifestations tend to cure, but a chronic squamous condition often supervenes, with recurrences of vesiculation. In all forms of the disease, particularly the vesicular, erythematopapular or erythematous-squamous eruptions may spread up as far as the knees (Korne, 1934).

Where many cases of fungus infection are being seen, an unwarranted clinical diagnosis may be made, and there are lesions clinically typical of epidermophytosis in which a fungus cannot be demonstrated. Various micrococci have been found (Sabouraud, 1910, 1923; Hulsey and Jordan, 1925), and it is necessary to concede that bacteria are solely responsible for some cases of so-called ringworm of the feet (Weidman, 1927). If a pathogenic and hæmolytic streptococcus is present "it is there for business and not as an innocent bystander" (Mitchell, 1935), and Greenwood (1922) state that while the staphylococcus may be present on normal skins the finding of a streptococcus is of ætiological significance. Andrews *et al.* (1934) have described a series in which pustular conditions of the soles were due to focal infections, while pustular psoriasis (Barber, 1933) is subject to periods of quiescence and exacerbation and, as the sides of the toes may be involved, with sodden peeling, may well be confused with epidermophytosis. The toes and feet may show ringworm-like lesions in generalized eruptions, such as seborrhœic and other forms of dermatitis, psoriasis, and lichen planus and even pityriasis rosea (Weiss *et al.*, 1927). A dermatitis may be caused by the dye in socks, or tanning agents or leather dyes in shoes, or by the application of such agents as iodine to abrasions, &c. Perionychia may be due to fungus infection but it can be pyogenic, tuberculous or syphilitic. Secondary syphilis may produce condylomata between the toes in the form of messy, scaly, slightly purulent lesions. Cases of simple dyshidrosis are often regarded as mycotic. In this condition non-inflamed, deep, uniform sago-grain-like vesicles spring up at once symmetrically in dozens or hundreds, burning rather than itching, seldom rupturing spontaneously, and showing no marginal activity or surrounding collar (Scholtz, 1932). No fungus elements are found in the roofs of the vesicles. Cases of localized hyperhidrosis as described by Tobias (1927) are very rare. Hyperkeratosis of the soles may occur in tertiary syphilis, keratoderma blennorrhagica, and following the administration of arsenic.

On February 11, 1937, Heggs delivered a Chesterfield Lecture on skin diseases of the feet and I have used notes of that lecture.

Following the work of Strickler (1916) on the differential diagnosis of ringworm and other skin infections by the results of white blood-cell counts, I have carried out this examination in 100 successive cases of epidermophytosis of the feet, using patients with other skin diseases and normal skins as controls. I found no constant factor present which would aid.

No discussion of this disease would be complete without mentioning the secondary eruptions, known as epidermophytides, epidermophytids, or simply as "ids" which occur usually on the hands but also on other parts of the skin surface as a concomitant to fungus lesions between the toes and on the feet. They were first described by Jadassohn in 1912 and investigated in the United States more particularly, though Cranston Low in Scotland gave a detailed account in 1924. The concept is now generally accepted by dermatologists but the subject remains controversial. I have seen 34 patients with dyshidrotic or squamous eruptions on the hands, and others with erythematous and papular lesions elsewhere, for which no other cause could be found than that of an allergic response to a primary fungus lesion of the skin of the feet. Authoritative articles have been written by Williams (1922, 1926, 1927), Strickler *et al.* (1932), Sulzberger (1936), and Peck (1937). The phenomenon can be compared to the action of bacteria, which, locked up in various organs, act as local foci of infection and cause urticaria, &c. There is similarity between the secondary eruptions due to fungi and certain of the tuberculides and secondary syphilitic eruptions. The fungus has been found in the blood-stream in man. It is necessary for the fungus or its products to reach and invade the living part of the skin to produce sensitivity and resulting allergic manifestations (Peck, 1937), and it is suggested that keratolytics, strong antiseptics, X-rays, &c., may force the fungi or their products into the blood-stream, or sensitize tissue in themselves or prepare the way for sensitization by other substances. It has been discussed whether the presence of a fungus

infection may sensitize the patient to other substances than the toxin of the fungus concerned, such as occupational irritants (White and Taub, 1932; Goldsmith, 1936). The fungus is rarely found in secondary lesions and this has been variously explained (Williams, 1927; Cleveland White, 1929). Peck (1937) gives criteria which must be satisfied before a diagnosis of an "id" can be made, and strictly speaking these should be satisfied, but this is difficult when no laboratory is available. From the clinical point of view it is necessary to eliminate such causes as a primary mycotic infection, drug and food rashes, local irritants such as iodine, occupational causes, and bacterial foci of infection in the body or on the skin surface. A careful history should be taken to make sure there has been no nervous upset, and the question of a personal or family history of asthma, &c. must be considered (Wise and Wolf, 1936; McLachlan and Brown, 1934; Bauckus and Siekmann, 1936). An "id" may simulate skin conditions due to all these causes. If no such cause can be found after exhaustive search it is thought that a diagnosis of a secondary fungus infection may be made.

Many types of epidermophytide are described (Cranston Low, 1924; Peck, 1937). Cheiropompholyx-like eruptions are the most common in my experience. Treatment should be directed to the primary lesion, and the "id" soothed with zinc or calamine cream. Cure of the epidermophytosis is followed by cure of the epidermophytide.

Treatment by trichophytin extract "remains a nebulous terrain" (Wise, 1936), and many writers report varying degrees of success (Peck, 1930; Van Dyck *et al.*, 1931; Sulzberger and Wise, 1932; Robinson and Grauer, 1935; Traub and Tolmach, 1935).

Epidermophytosis of the skin of the feet is difficult to cure and liable to relapse or recur, but it is not incurable if a suitable remedy is found, persisted in long enough—the average case requiring at least three months' treatment—and precautions taken to render the sites of infection unsuitable for the growth of fungi. No patient is cured who does not show normal skin with negative fungus findings, and even then prognosis should be guarded. Fungi have been found in apparently normal skin 1 to 2 in. beyond active lesions, and this must be remembered in applying remedies.

The disease has been treated by every conceivable drug and therapeutic agent (Goodman, 1931). Everything has been tried from kerosene to chiropractic (Barksdale, 1933). The general condition should be treated with tonics and a generous, high-vitamin-content diet. Local applications should never irritate, particularly with inflammation present. If the skin is irritated the lesions spread, become temporarily intolerant to curative applications and are likely to relapse (Toomey, 1930), while allergic manifestations are more likely to appear (Maschkilleisson *et al.*, 1934). Frankly secondarily infected patients should be treated in bed, and boric starch poultices, eusol soaks, &c. applied on the usual lines, as much debris and dead skin as possible being removed by bathing and mechanical means, care being taken to avoid trauma to living tissue. When inflammation is not present, or has been relieved, it is necessary to find a suitable remedy, remembering that individual skins react differently to different agents and that the right application may be found only by trial and error, discontinuing the use of any which cause irritation and gradually reducing the strength of preparations found suitable.

A remedy should possess the following properties:—

It should kill or check the growth of the fungus; should penetrate to the fungus in a normal or pathologically altered structure of the epidermis; should not harm the skin; should not have an unpleasant smell; should preferably be colourless, not spoil the clothes, and be cheap; should, if possible, counteract predisposing factors, such as sweating and lowered acidity (Bonnevie, 1936).

I have had the opportunity to treat over 1,000 cases of the disease during the last ten years, and in my experience the following general lines of treatment have been the most successful:—

Intertriginous types.—(1) With gross maceration: Twice daily the feet are bathed

in a lotion for half an hour and afterwards carefully dried and powdered. (2) Acute and subacute cases: Every night an ointment is rubbed into and around the infected areas. Next morning the ointment is wiped off, the feet bathed in a lotion and a paint applied to the lesions. At bedtime the feet are again bathed, dried, and the ointment applied. (3) Chronic cases: As for acute and subacute cases but a special paint containing a copper salt is used.

Vesiculo-bullous types.—All vesicles and bullæ are opened twice daily with a sterile needle and a paint applied. If the surface of the lesion becomes raw and weeping the paint is discontinued and lotions alone are used, while, if the surface becomes scaly, an ointment is substituted for the paint.

Hyperkeratotic types.—A paste is applied twice daily but never for longer than five days at a time, with gradual reduction in the strength as peeling becomes established. If irritation occurs a soothing calamine cream is applied.

Fissures should be painted with silver nitrate 1% to 5% in nitrous spirit of ether. Toomey (1930) uses a 10% solution. Sharlitt (1935) recommends 1% tetraiodo-methenamine, salicylic acid, and thymol in collodion flexile.

I now propose to state the preparations which I use of choice, and to discuss these and others which have been recommended and tried, mentioning that amazing differences in success are obtained with different remedies in various hands.

(1) *Powders.*—(a) 1% salicylic and benzoic acids and 5% boric acid in talc.

(b) Mycozol dusting powder.

(2) *Lotions.*—(a) Potassium permanganate, 1:4,000.

(b) Abracide skin lotion, 1:100.

(3) *Ointments.*—(a) Whitfield's ointment. (Often wrongly prescribed.)

R	Acidi benzoici	gr. 25
	Acidi salicyli	gr. 15
	Paraff. mollis	dr. 2
	Olei cocois nucis	oz. 1

15 gr. of hard paraffin should be added in hot weather.

(b) Mycozol.

(4) *Paints.*—(a) Liquid mycozol.

(b)

R	Acidi benzoici	dr. 1½
	Acidi salicyli	dr. 1
	Acetone	oz. 1
	Spiritus vini meth.	oz. 4

(c)

R	Hydrarg. perchloridi	gr. 1
	Acidi salicyli	gr. 10
	Olei ricini	℥ 10
	Spiritus vini meth.	oz. 1

(d)

R	Cupri nitratis	gr. 40
	Acidi benzoici	dr. 1½
	Acetone	dr. 1½
	Spiritus vini meth.	oz. 5
	Aq. destillata	8oz.

The last lotion is recommended by Whitfield (1934).

Salicylic acid has a fungicidal action (Sharlitt, 1935), and is keratolytic. If used in too strong concentrations it will crack the skin (Skeoch, 1928), and in some patients it causes a mild dermatitis. In hyperkeratotic cases it can be used in the form of a paste, in strengths as high as 2 drachms to an ounce of soft paraffin. It is an extremely valuable remedy.

Carbolfuchsin, either alone or as Castellani's paint, gentian violet, malachite, and brilliant green are dyes which have been used with success. Malachite green is now most commonly applied and is an active fungicide (McCrea, 1934). It is contained in liquid mycozol. Chrysarobin has been recommended (Skeoch, 1928; Hallows, 1936). Apart from its staining properties, it may cause dermatitis (Stevenson, 1929), and should be used with caution. Cignolin, which is chrysarobin minus the methyl group, and stronger, can be made up as an ointment or paint (Manson-Bahr, 1935), and gives good results. Kenedy (1931), recommends a paint containing cignolin, gr. $\frac{1}{2}$ and oil of cade, $\text{m}l$ 40 in rectified spirit, oz. 1 in chronic cases. Buchbinder (1934), and Jones (1935), have faith in abracide skin lotion, which I also use. In addition to the lotion and powder an ointment is produced. Iodine is a fungicide (Schamberg *et al.*, 1931) and has some therapeutic value (Strickler, 1933; Legge *et al.*, 1934). It often irritates and in my experience causes secondary manifestations. Its use is apt to produce the "brown mess" on the skin described by Haldin-Davis (1930). According to Wigley (1936), the preparation called paranitrophenol gives encouraging results, while Lomholt (1934) recommends mycoctenol, the ethyl ester of paraoxybenzoic acid, in 5% solution in spirit or as an ointment as a clean, convenient, and non-staining remedy. Mercurochrome 220 soluble is most disappointing and I have ceased to use it. Gomez-Vega (1936) was impressed by its use in conjunction with "visible light". Mention is made of the application of pine oil (Smyth and Smyth, 1932), bismuth violet (Barksdale, 1933), tetrachlorophenol sodium (Weider, 1935), chinisol (Lortat-Jacob and Bridault, 1926), and thymol and cinnamon (Myers and Thienes, 1925). Belisario (1935) has had successes by applying citric acid several times daily. Unusual methods of treatment suggested are the intravenous injection of Lugol's iodine (Doug-Ngoc-Dieu, and Millous, 1923), the inhalation of ethyl iodide (Swartz, 1935), and the attraction of fungi to the surface where they can be better attacked by the application of packs of Sabouraud's medium (Williams, 1936b). The correction of orthopaedic abnormalities should be regarded as an important part of treatment (Lieberthal, 1934).

This is not a complete survey of therapeutic measures. It is necessary to "go slowly" and keep on long after apparent cure is achieved. The war against the fungus should be one of attrition rather than a series of spectacular and spasmodic attacks.

X-rays do not kill the ringworm fungus but simply bring out the hairs affected by the disease (Gray, 1935). If carefully given in fractional doses, however, treatment by X-rays is claimed to facilitate cure (Ingram, 1935), and to shorten the course of epidermophytosis in some cases (McGlasson and Lehman, 1924). At least it gives symptomatic relief. Treatment with the so-called Grenz rays has proved disappointing (Dorne and Cleveland White, 1931).

Fungus infection of the nails is regarded as a common source of re-infection and relapse in adjacent skin surfaces (Hodges, 1921; Williams, 1928; Williams and Barthel, 1929; Rockwood, 1930). It is wellnigh impossible to cure. Treatments suggested are evulsion under anaesthesia (Whitfield, 1923), the application of double-strength Whitfield's ointment under adhesive tape (Whitfield, 1934), the use of Fehling's solution (Gardiner, 1931), and the painting of the nails with carbolfuchsin to which 2.5% salicylic acid has been added (Hasson, 1934).

To prevent the occurrence and spread, general and individual precautions can be taken. The site should be rendered unsuitable for the fungus to work in (Gray, 1934). There has been a tendency to chase the fungus and forget foot hygiene (McCormick, 1935).

The clothing of an infected patient should be disinfected. Clothes should be efficiently washed and efficiently dried, steam laundries being utilized as much as possible. In ships, despite regulations, clothes are often hung up to dry in steamy, unauthorized places, and socks, particularly if woollen, put on while still damp.

Whenever possible, socks should be put out in the open air to dry in the sun. Bathrooms, ashore and afloat, should be efficiently ventilated to avoid "steaminess," and their floors, and those of dressing rooms and cubicles, tiled, and scrubbed daily, soap powder being used; mere flushing is not sufficient (Greenwood, 1935). All forms of bath-mat which cannot be sterilized should be avoided, and efficient drainage should be provided for shower baths. Community bathrooms should contain pans containing 0.5 to 1% sodium hypochlorite for bathing the feet, and a suitable powder for dusting between the toes. In the Services, schools, &c., occasional inspections of the feet could be carried out, and lectures given and notices posted regarding the nature of the disease and the essentials of foot hygiene.

Particularly in hot weather, boots and shoes should be light and loose-fitting and should not be worn next to the skin. The leather should be vegetable—as opposed to chrome—tanned. White canvas shoes are preferable to those of "buckskin". The wearing of sandals can be encouraged, and crêpe-soled, rubber—and imitation rubber—soled shoes avoided, with the wearing of "gym" shoes cut down to a minimum. The toes ought not to be crowded by tight foot-wear. Men swabbing or scrubbing decks with strong alkaline solutions should not have bare feet. Boots and shoes can be disinfected from time to time by placing in the toes a pledget of cotton-wool soaked in formaline solution, and leaving overnight in a shoe box (Henderson, 1932; McCormick, 1934). They can be aired afterwards to avoid a dermatitis. Infected individuals should destroy bedroom slippers, if worn, and obtain new ones with loofah soles and bath-towel uppers. These can be boiled (Whitfield, 1934). Well-fitting, boilable, white cotton socks should be worn in hot weather and changed as often as possible. These can be worn under woollen socks when marching. These woollen socks can be disinfected by soaking in a solution of 1% thymol in spirit for one hour (Kadisch, 1931). Powdering inside the socks is helpful.

A towel belonging to someone else should never be used. Towels should be washed as often as possible and efficiently dried, and never, on any pretext, piled in heaps.

No one should walk bare-foot on floors, floor-coverings, or decks, particularly in bathrooms, matsheds, dressing rooms, cubicles, &c. After bathing it is easy to dry the feet without placing a bare foot on the floor if slippers are placed within convenient reach. Germicidal soaps such as "neko" can be used for washing the feet but strong caustic soaps must be avoided. After bathing in salt water, the feet should be immersed in fresh water, whenever possible, and sand particles washed away. Scrupulous drying of the feet, particularly between the toes, after bathing, is the most important factor in prevention. After this careful drying, a powder—not containing starch, which "cakes"—should be dusted over the feet and between the toes. Boric acid in finely powdered talc, silatox, or the well-known "baby" powders are excellent for the purpose. "Fungicidal" powders are not suitable, as a dermatitis might be caused if they were used for the long periods necessary. The toilet procedure of powdering between the toes should become as much a matter of routine as cleaning the teeth, and the tin of powder as necessary a constant companion as the tooth-brush.

In cases of excessive sweating it may be advisable to add for a time 1% salicylic acid to the powder and to bathe the feet in weak solutions of alum or potassium permanganate. Witch-hazel and cologne water are also useful, while in severe cases Gilman (1935) recommends 4% salicylic acid and 8% resorcinol in alcohol at night, with a powder by day.

REFERENCES

- ANDREWS, G. C., BIRKMAN, F. W., and KELLY, R. J. (1934), *Arch. Dermat. and Syph.*, N.Y., **29**, 548.
BARBER, H. W. (1933), *Brit. J. Dermat.*, **45**, 113.
BARKSDALE, I. S. (1933), *Med. J. and Record*, **138**, 279.
BAUCKUS, H. H., and SIEKMANN, C. F. (1936), *N.Y. State J. Med.*, **36**, 159.
BELISARIO, J. C. (1935), *Med. J. Australia*, **11**, 513.

- *BONAR, L., and DREYER, A. D. (1922), *Am. J. Pub. Health*, **22**, 909.
 BONNEVIE, P. (1936), *Acta dermat.-venereol.*, **17**, 576.
 BUTCHINDER, J. H. (1934), *Med. Rec.*, **139**, 286.
 BUTLER, C. S., HOUGHTON, J. E., and COOPER, G. F. (1934), *U.S. Nav. M. Bull.*, **21**, 615.
 *BUTLER (1935), *Med. J. Australia*, **11**, 513.
 CANTOR, M. J. (1936), *N.Y. State J. Med.*, **36**, 773.
 CORNBLEET, T. (1936), *Arch. Dermat. and Syph.*, N.Y., **15**, 670.
 Id. (1934), *ibid.*, **29**, 887.
 CUMMING, H. S. (1928), *U. S. Pub. Service Health News Bull.*, E.28.
 DORNE, M., and WHITE, CLEVELAND (1931), *Arch. Dermat. and Syph.*, N.Y., **24**, 409.
 DOUG-NGOC-DIEU, and MILLOUS, P. L. G. (1923), *Paris méd.*, **13**, 88.
 FLYNN, J. W. (1935), *Med. J. Australia*, **11**, 513.
 FRANKLIN, J. L. (1935), *Practitioner*, **135**, 298.
 GARDINER, F. (1931), "Handbook of Skin Diseases", Edinburgh, p. 99.
 GILMAN, R. L. (1935), *J.A.M.A.*, **100**, 715.
 GLAZE, A. (1924), *South M. J.*, **17**, 643.
 GOLDSMITH, H. W. N. (1936), *Brit. J. Dermat.*, **48**, 593.
 GOMEZ-VEGA, P. (1936), *Arch. Dermat. and Syph.*, N.Y., **34**, 961.
 GOODMAN, H. (1931), *Arch. Dermat. and Syph.*, N.Y., **23**, 872.
 *GOULD, W. L. (1931), *J.A.M.A.*, **96**, 1300.
 GRAFFENBIEDE, C. von (1918), *Dermat. Wchnschr.*, **6**, 361.
 GRAHAM-LITTLE, E. (1916), *St. Mary's Hosp. Gazette*, **22**, 124.
 GRAY, A. M. H. (1927), *Arch. Dermat. and Syph.*, N.Y., **15** (In discussion).
 Id. (1934), *Brit. M. J.* (ii), 541.
 Id. (1935), *Practitioner*, **135**, 59.
 GREENWOOD, A. M. (1935), *New England J. Med.*, **213**, 363.
 GREENWOOD, A. M., and SWARTZ, J. H. (1927), *Arch. Dermat. and Syph.*, N.Y., **15**, 404.
 GUY, W. H., and JACOB, F. M. (1923), *Pennsylvania M. J.*, **26**, 384.
 HALDIN-DAVIS, H. D., (1930) "Modern Skin Therapy", London, p. 41.
 HALLAM, R. (1928), *Brit. M. J.* (i), 835.
 HALLEWS, N. (1922), *Lancet* (ii), 791.
 Id. (1936), *ibid.* (ii), 188.
 HASSON, J. (1934), *Brit. M. J.* (ii), 928.
 HENDERSON, Y. (1932), *Arch. Dermat. and Syph.*, N.Y., **26**, 710.
 HODGES, R. S. (1921), *ibid.*, **4**, 1.
 *HULSEY, S. H., and JORDAN, F. M. (1925), *Am. J. M. Sc.*, **169**, 267.
 INGRAM, J. T. (1935), *Practitioner*, **135**, 475.
 JADASSOHN (1912), quoted by SULZBERGER, M. B. (1929), *Arch. f. Dermat. u. Syph.*, **157**, 345.
 JAMIESON, R. C., and MCCREA, A. (1932), *Arch. Dermat. and Syph.*, N.Y., **25**, 321.
 Id. (1937), *ibid.*, **35**, 203.
 JONES, C. C. (1935), *J. Roy. Army M. Corps*, **65**, 306.
 KADISCH, E. (1931), *Derm. Wchnschr.*, **37**, 1433.
 KENEDY, D. (1931), quoted in *Lancet* (ii), 754.
 KORNE, F. (1934), *South African M. J.*, **8**, 244.
 LEGGE, R. T., BONAR, L., and TEMPLETON, H. J. (1929), *J.A.M.A.*, **92**, 1507.
 Id. (1934), *Arch. Dermat. and Syph.*, N.Y., **29**, 520.
 LEVIN, O. L., and SILVERS, G. H. (1932), *Arch. Dermat. and Syph.*, N.Y., **25**, 466.
 LIEBERTHAL, D., and LIEBERTHAL, E. P. (1934), *ibid.*, **29**, 356.
 LOMHOLT, S. (1934), quoted (1935), *Brit. J. Dermat.*, **47**, 310.
 LORTAT-JACOB, L., and BRIDAULT, C. (1926), *Bull. Soc. franç. de dermat. et syph.*, **33**, 719.
 LOVEJOY, E. D. (1923), *California State J. Med.*, **21**, 380.
 LOW, R. CRANSTON (1924), "Anaphylaxis and Sensitization", Edinburgh, p. 152.
 MACLEOD, J. M. H. (1928), *Brit. M. J.* (i), 656.
 MCCORMICK, W. J. (1934), *Canad. J. Med. and Surg.*, **75**, 134.
 Id. (1935), *Canad. Pub. Health J.*, **26**, 281.
 MCCREA, A. (1934), *Mycologia*, **26**, 5.
 MCGLOSSON, I. L., and LEHMANN, C. F. (1924), *Texas State J. Med.*, **19**, 626.
 MCLACHLAN, A. D., and BROWN, W. H. (1934), *Brit. J. Dermat.*, **46**, 457.
 MANSON-BAHR, P. (1935), "Manson's Tropical Diseases", London, p. 639.
 MARCHIONINI, A. (1929), *Dermat. Ztschr.*, **56**, 248.
 Id. (1930), *ibid.*, **58**, 222.
 MASCHKILLEISSON, L. N., SEGAL, M.B., and SIGALOWA, E. E. (1934), *Acta dermat.-venereol.*, **15**, 300.
 *MEDICAL RESEARCH COUNCIL (1931), "System of Bacteriology in Relation to Medicine", vol. 8.
 MILOCHEVITCH, S. (1936), *Dermat. Wchnschr.*, **102**, 320. Quoted *Brit. J. Dermat.* 1937, **49** 44.
 MITCHELL, J. H. (1935), *J.A.M.A.*, **104**, 1220.
 MOORE, M. (1936), *Arch. Dermat. and Syph.*, N.Y., **34**, 880.
 MUENDE, I. (1934), *Brit. J. Dermat.*, **46**, 479.
 MUSKATBLIT, E. (1933), *New York State J. Med.*, **33**, 632.
 MYERS, H. B., and THIENES, C. H. (1925), *J.A.M.A.*, **84**, 1935.
 ORMSBY, O. S. (1935), "Diseases of Skin", London, p. 969.
 ORMSBY, O. S., and MITCHELL, J. H. (1916), *J.A.M.A.*, **67**, 711.
 *OSBORNE, E. A., and HITCHCOCK, R. S. (1931), *ibid.*, **97**, 453.
 PRICK, S. M. (1930), *Arch. Dermat. and Syph.*, N.Y., **22**, 40.
 Id. (1937), *New York State J. Med.*, **36**, 1237.
 *PRIESTLEY, H. (1937), *M. J. Australia*, **2**, 471.
 ROBINSON, G. H., and GRAUER, R. C. (1935), *Arch. Dermat. and Syph.*, N.Y., **32**, 787.

- ROCKWOOD, E. M. (1930), *ibid.*, **22**, 359.
 ROXBURGH, A. C. (1931), "Common Skin Diseases", London, p. 122.
 SABOURAUD, R. (1910), *Ann. de dermat. et syph.*, Paris **1**, 289.
 Id. (1923), *ibid.*, **4**, 425.
 SCHAMBERG, J. F., BROWN, H., and HARRIS, M. J. (1931). *Arch. Dermat. and Syph.*, N.Y., **24**, 1033.
 SCHOLTZ, M. (1932), *Arch. Dermat. and Syph.*, N.Y., **25**, 812.
 SEMON, H. (1934), *Lancet* (i), 530.
 SHARLITT, H. (1935), *Arch. Dermat. and Syph.*, N.Y., **31**, 217.
 * SHARP, W. B., and TAYLOR, E. K. (1928), *J. Prev. Med.*, **2**, 485.
 SKEOCH, H. G. (1925), *Brit. M. J.* (i), 895.
 SMYTH, H. F., and SMYTH, H. F., JR. (1932), *Arch. Dermat. and Syph.*, N.Y. **25**, 1079.
 STEVENSON, J. (1929), *J. Oklahoma M. A.*, **22**, 113.
 STRICKLER, A. (1916), *J. Cutaneous Dis.*, **34**, 752.
 Id. (1933), *Arch. Dermat. and Syph.*, N.Y., **28**, 836.
 STRICKLER, A., and FRIEDMAN, R. (1931), *ibid.*, **24**, 430.
 STRICKLER, A., and MCKEEVER, W. W. (1934), *ibid.*, **29**, 526.
 STRICKLER, A., OZELLERS, E. A., and ZALATEL, R. P. (1932), *ibid.*, **25**, 1028.
 SULZBERGER, M. B. (1936), *New England J. Med.*, **8**, 330.
 SULZBERGER, M. B., and WISE, F. (1932), *J.A.M.A.*, **99**, 1759.
 SWARTZ, J. H. (1935), *Arch. Dermat. and Syph.*, N.Y., **32**, 551.
 Id. (1936), *New England J. Med.*, **8**, 322.
 TOBIAS (1927), *Arch. Dermat. and Syph.*, N.Y., **15**, 511.
 TOOMEY, N. (1930), "Treatment of Skin Diseases", St. Louis, U.S.A.
 TRAUB, E. F., and TOLMACH, J. A. (1935), *Arch. Dermat. and Syph.*, N.Y., **32**, 413.
 VAN DYCK, L. S., KINGSBURY, J., THORNE, R., and MYERS, C. N. (1931), *New York State J. Med.*, **31**, 611.
 WEIDER, L. M. (1935), *Arch. Dermat. and Syph.*, N.Y., **31**, 644.
 WEIDMAN, F. D. (1927), *ibid.*, **15**, 415.
 Id. (1928), *J.A.M.A.*, **90**, 499.
 WEISS, R. S., LANE, C. W., and SHOWMAN, W. A. (1927), *Arch. Dermat. and Syph.*, N.Y., **15**, 304.
 * WHITE, CLEVELAND (1928), *J.A.M.A.*, **90**, 1865.
 Id. (1929), *Arch. Dermat. and Syph.*, N.Y., **20**, 315.
 WHITE, C. J. (1927), *Arch. Dermat. and Syph.*, N.Y., **15**, 378.
 WHITE, C. J., and TAUB, S. J. (1932), *J.A.M.A.*, **13**, 524.
 WHITFIELD, A. (1906), *Lancet* (ii), 237.
 Id. (1923), *ibid.* (i), 1124.
 Id. (1934), *J. Trop. Med.*, **37**, 353.
 WIGLEY, J. E. (1936), *Practitioner*, **146**, 541.
 WILLIAMS, C. M. (1922), *Arch. Dermat. and Syph.*, N.Y., **5**, 161.
 Id. (1926), *ibid.*, **13**, 661.
 Id. (1927), *ibid.*, **15**, 451.
 Id. (1928), *ibid.*, **18**, 730.
 WILLIAMS, C. M., and BARTHEL, E. A. (1929), *J.A.M.A.*, **93**, 907.
 WILLIAMS, J. W. (1936), *Arch. Dermat. and Syph.*, N.Y., **33**, 335.
 Id. (1936b), *J. Lab. and Clin. Med.*, **23**, 268.
 WISE, F. (1936), *Arch. Dermat. and Syph.*, N.Y., **33**, 356.
 WISE, F., and WOLF, J. (1936), *ibid.*, **34**, 1.
 Id. (1936), *J.A.M.A.*, **107**, 1126.

* Not referred to in Paper, as abbreviated.

Dr G. ROME HALL: At Lagos, in 1893, civilian Hauzzas were treated for what was then known as "ainum", described as a circular rodent ulcer around the base of the little toe. Sometimes the whole of the ligaments around the metacarpophalangeal joint were exposed; they came for removal of the moribund toe. One point to note is that they were a people who wore sandals; the ulcer was always fouled with sand. Often they were newcomers from the interior, living on an altered dietary.

I was on service at a mine in the forest rain-belt zone of the Gold Coast for several months in 1933, the middle months of which were specially unhealthy owing to excess of rain and want of sun. Despite all usual care a personal attack of dhubie itch eczema occurred, one cause of which was being often three hours in perspiration-laden clothes in the morning. Investigation showed that half the Europeans had been served for months, by lazy houseboys, with condensed water for drinking and cooking, and thus a calcium deficiency had been caused.

Stress has been laid on the occurrence of these mycotic diseases at the age of puberty, a time when there is a special need for calcium. It has also been emphasized that they attack middle-class schools; the pupils in these schools are just the persons who go in for bathing, thus incurring damp and not fully dried feet.

Section of Epidemiology and State Medicine

President—Surgeon Rear-Admiral SHELDON F. DUDLEY, O.B.E.

[April 9, 1937]

Active Immunization against Diphtheria by the Combined Subcutaneous and Intranasal Method

By CLAUS JENSEN, M.D.

(Director, Department of Biological Standards)¹

INTRODUCTION

IN view of the important contributions to the subject of active immunization against diphtheria which have been made by English investigators, notably by Glenny and his colleagues (1921), Forbes (1932), Dudley and his collaborators (1934), and many others, it is with some diffidence that these results are presented. They must be regarded as a small contribution to a subject which, on account of the intensive study it is receiving in many countries, is in a state of exceptionally rapid growth and development. Moreover, even a review of the extensive literature on the subject cannot be attempted in this paper; the main facts and opinions are, however, well known to workers in this field.

I shall therefore only mention the more recent works which have a direct bearing on our investigations in Denmark, and express the hope that this will not be misinterpreted. I should like to emphasize that I fully acknowledge all the former work done in this field, and that the results which I am now communicating should be considered only as a link in the series of all the previous investigations.

The actual number of individuals inoculated against diphtheria in Denmark is relatively small. This fact is not due to failing interest in the problem on the part of the health authorities or the Statens Serum Institut, but to two other circumstances:—

- (1) The number of diphtheria cases in Denmark has been very low for some years;
- (2) The health authorities and the Statens Serum Institut have deliberately refrained from a propaganda until we were in possession of the most effective, harmless, and suitable method for mass-immunization against diphtheria.

In some countries, mass-immunization by the original procedure of three injections, recommended by Ramon, has been possible, and this procedure seems to induce immunity in from 90 to 95% of the individuals receiving *all* three injections. There are, however, several well-known drawbacks to the three-injection method.

Much of the recent work has therefore been directed towards the production of a diphtheria antigen which, while being absolutely safe and free from the property of causing undue local and general reactions, is of such high immunizing efficiency that mass-immunization can be successfully achieved by the administration of a single subcutaneous injection. This perfect antigen has not yet been produced, but it is submitted that the results obtained in Denmark during the past few years mark a stage forward towards the realization of this ideal.

In most field investigations either the statistical method or the Schick test method has been used to evaluate and compare the results obtained in the active immunization of human beings on a large scale. Each of these methods has its merits and its

¹ From Statens Serum Institut (Director: Dr. Th. Madsen), Copenhagen.

defects; a discussion of these is not relevant to the subject of our investigations, but will be given in a subsequent paper.

In Denmark the method of the *quantitative determination of the antitoxin response* (Claus Jensen, 1933 *a* and *b*) has been used in order to evaluate the results of the various active immunization procedures which have been studied.

The tables, graphs, and charts which follow show the antitoxin titre, of individuals or of groups, before treatment of any kind and the titres which are obtained at the periods stated after a particular immunization procedure has been applied.

THE NATURAL AND ARTIFICIAL ANTITOXIN SPECTRUM AS AN EXPRESSION OF THE IMMUNITY OF A POPULATION

The presence of even small amounts of natural antitoxin indicates that a secondary response will follow even a small antigenic stimulus. The immunizability of a population, therefore, will be directly correlated to the number of its individuals possessing natural antitoxin and also, to some extent, on the magnitude of this natural antitoxin.

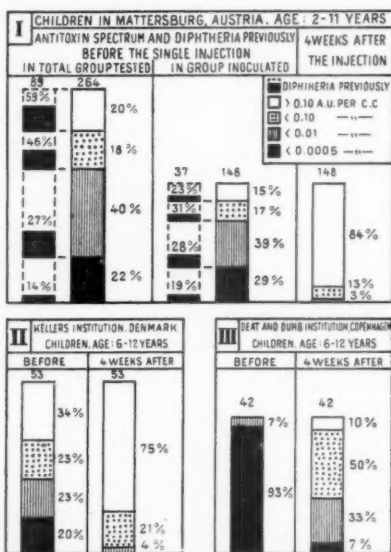


FIG. 1.—The natural antitoxin spectrum of three different groups of children and their response to a single subcutaneous dose of purified $Al(OH)_3$ -toxoid as expressed by the artificial antitoxin spectrum four weeks after the injection.

A good expression of the immunity and immunizability of a population might therefore be obtained by grouping its individuals according to the titres found in the primary blood samples.

Based on our experience from more than 3,000 primary blood samples from children and adults, we have found it most useful to employ the following sub-groups:—

- (1) Individuals with less than 0.0005 A.U. per c.c. serum.
- (2) Individuals with more than 0.0005 but less than 0.01 A.U. per c.c. serum.
- (3) Individuals with more than 0.01 but less than 0.10 A.U. per c.c. serum.
- (4) Individuals with 0.10 A.U. or more per c.c. serum.

This division of a group of children or adults into sub-groups has been represented graphically in the way illustrated in fig. 1.

It is convenient and adequate to term the herd-immunity and immunizability established in this way as the *antitoxin spectrum of the population* investigated.

We may accordingly speak of the *natural or primary antitoxin spectrum* of a population, which would indicate its original or basic immunity or immunizability as expressed by the distribution of natural antitoxin in the group at the time when the primary blood samples were taken, and in the same way, the term *artificial or secondary antitoxin spectrum* would express the immunity of the group after inoculation.

There is an essential difference between the natural and the artificial antitoxin spectrum, which should be emphasized.

The natural antitoxin spectrum represents the immunity or immunizability of a population and may, of course, show variations from time to time, in relation to the fluctuations in the frequency of specific environmental stimuli in the community. It represents, however, more or less a state of equilibrium, whereas the artificial antitoxin spectrum, which is usually established at its best when the individual antitoxin titres are at their maximum, illustrates a much more unstable condition. In the absence of further antigenic stimuli, it will at first change considerably, i.e. the antitoxin spectrum will become poorer as some of the individuals in the dotted and striped groups relapse into the striped and black groups respectively. For this reason, the individuals in the striped group in the natural antitoxin spectrum cannot be compared with the same group in the artificial spectrum. The latter group may not be regarded as safely immunized.

According to its composition and the size of the various sub-groups, the antitoxin spectrum may be termed "good", "medium", or "poor". The extremes would be represented by a completely white or completely black spectrum and the intermediate stages by spectra more or less rich in shades respectively. The three natural antitoxin spectra given in fig. 1 may well serve as examples. The child population in Mattersburg shows a good spectrum, whereas in the two communities of institutional children in Denmark, it may be termed excellent in Keller's Institution, but very poor in the Royal Institution for Deaf and Dumb Children.

The natural (and artificial) antitoxin spectrum may be said to reflect the past experiences of the individuals with the specific antigenic stimuli. A beautiful demonstration (fig. 1) of this was obtained in a joint investigation of the Health Division of the Rockefeller Foundation and Statens Serum Institut (Leach, Claus Jensen and Pösch, 1935) on a group of children in Mattersburg in Austria, where diphtheria had been very prevalent in the years just before the investigation.

In a group of 553 children (2-11 years old) inoculated with a single subcutaneous injection of purified $Al(OH)_3$ -toxoid, we succeeded in obtaining primary blood samples from 264. The natural antitoxin spectrum shows a high natural antitoxic immunity and immunizability of the child population. It resembles very much the artificial antitoxin spectrum of a population insufficiently immunized and is typical of a population in which diphtheria has been prevalent for some time, the characteristic feature being the dominance of the striped at the expense of the black.

The frequency distribution of previous diphtheria cases in the different sub-groups was then investigated. The circumstances were particularly favourable, as not less than 89, i.e. 33.7% of the children tested had had diphtheria one to three years previously. The result is given in the figure in the left, broken column. The correlation between the frequency of diphtheria previously and the magnitude of the natural antitoxin titre in the different sub-groups is very striking.

From the subsequent charts it will be evident that the natural antitoxin spectrum of the various groups of children and adults tested in Denmark, with one exception, may be termed as poor or mediocre; the exception is the excellent spectrum observed in the Keller Institution and is easily accounted for by the fact that in this community diphtheria had been endemic for some months prior to the examination.

ACTIVE IMMUNIZATION BY MEANS OF ONE INOCULATION

Much work has been undertaken in recent years to make this ideal of the public health administrator a practical procedure.

For some years, investigations with this object in mind have been carried out by S. Schmidt and his collaborators at Statens Serum Institut. The first step forward was made by S. Schmidt and Linderstrøm-Lang (1930), and later by S. Schmidt, A. Hansen, and K. A. Kjær (1931), who, by a method devised by Willstätter for the purification of enzymes, succeeded in producing highly purified and concentrated diphtheria formol toxoids containing up to 1,300 flocculation units (Lf) per c.c.

The results obtained in children (Claus Jensen, 1931, 1933a) with these preparations, though promising at first, were not satisfactory when tried on a large scale, possibly due to a too rapid elimination from the body, as the experiments of Glenny, Buttler, and Stevens (1931) suggest.

This was also indicated by the experiments of Glenny and Waddington (1929), who had found that the addition of alum greatly increased the immunizing power of toxoid in experimental animals and it has been shown later that various other substances have a similar effect (e.g. tapioca (Ramon, 1931), and calcium (Ramon and Nélis, 1932)).

The addition of these substances, however, often causes rather severe local reactions and sometimes abscess formation at the site of injection. These by-effects naturally reduce the value of such preparations in mass-immunization of children.

An effort to avoid these sequelæ was made by S. Schmidt (1932) who, in place of alum and crude toxoid, used the Willstätter preparation of aluminium-hydroxide and purified toxoid. As this preparation has a very high specific combining capacity for purified toxoid, it was considered that a small quantity might be sufficient to obtain the desired effect without giving severe or even moderate by-effects. The method of preparation of this antigen and the promising results of animal experiments have been published by S. Schmidt and A. Hansen (1933).

A single injection of Schmidt's purified toxoid¹ was first used as an immunizing agent on Danish children by Claus Jensen, K. Bojlén, and S. Ahrend Larsen (1931-33), and later by Leach, Claus Jensen, and Pösch (1935), on children in Austria.

Space will not allow a detailed account of these investigations here. It will be sufficient to illustrate the results obtained by a series of charts.

For how long a period will the purified $Al(OH)_3$ -toxoid continue to exercise an antigenic effect after the injection into children? In collaboration with Dr. Otto Kirstein, we have been able to follow the antitoxin production curve in four children after a single subcutaneous injection. It will be noticed from fig. 2 that antitoxin production starts between the tenth and twenty-first day and, in the good responder, No. 24, the maximum is reached about three weeks after the injection, whereas in the poor responders it occurs somewhat later.

From the antitoxin production curves demonstrated it is evident that antitoxin production starts fairly early. This is also shown by the response (fig. 3) in two groups of probationers. In one group the artificial antitoxin spectrum is shown two weeks after, and in the other four weeks after the injection.

That our preparation seems to act as an antigenic stimulus for more than four weeks is also supported by the results given in fig. 4.

Seven weeks after the injection all individuals have shown antitoxin production, whereas four weeks after the injection 10% have failed to do so.

Our observations indicate therefore, that a *single subcutaneous injection in children acts as a continuous antigenic stimulus for at least from three to five weeks.*

¹ All the preparations employed in these investigations were kindly made for us by S. Schmidt and his collaborators, and we take this opportunity to express our gratitude for the very valuable help and advice they have given us in this work.

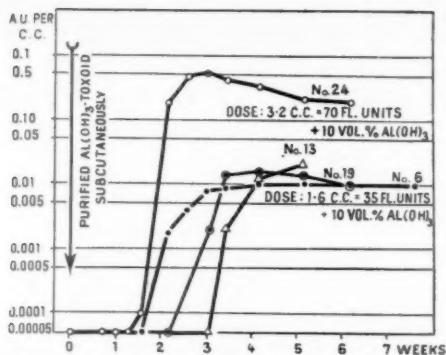


FIG. 2.—The response to a single subcutaneous injection of purified Al(OH)_3 -toxoid in four children (8 to 10 years of age) without detectable antitoxin (i.e. less than 0.00005 units per c.c. serum) prior to the injection.

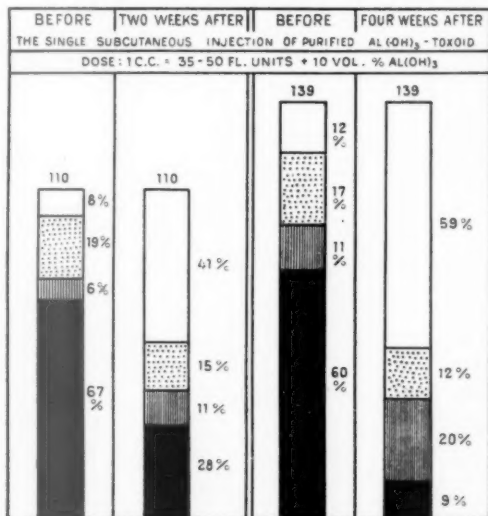


FIG. 3.—The antitoxin response in two groups of probationers two and four weeks after the single injection of purified Al(OH)_3 -toxoid.

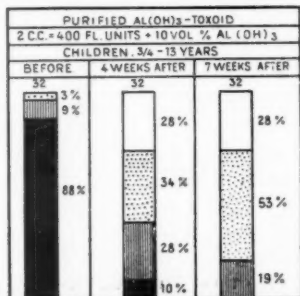


FIG. 4.—The antitoxin response in children to a large dose of purified Al(OH)_3 -toxoid, four and seven weeks after the single injection.

The antitoxin response in children and adults to a single injection of purified $Al(OH)_3$ -toxoid in increasing doses.—I should like first to call attention to the natural antitoxin spectra shown in fig. 5, which generally may be called mediocre or poor in the various groups of children and nurses in Denmark, although the majority of the children are 6 to 7 years of age.

Even the probationers, who are practically all 25 years of age, have a very poor natural antitoxin spectrum. These findings may be said to be characteristic of the

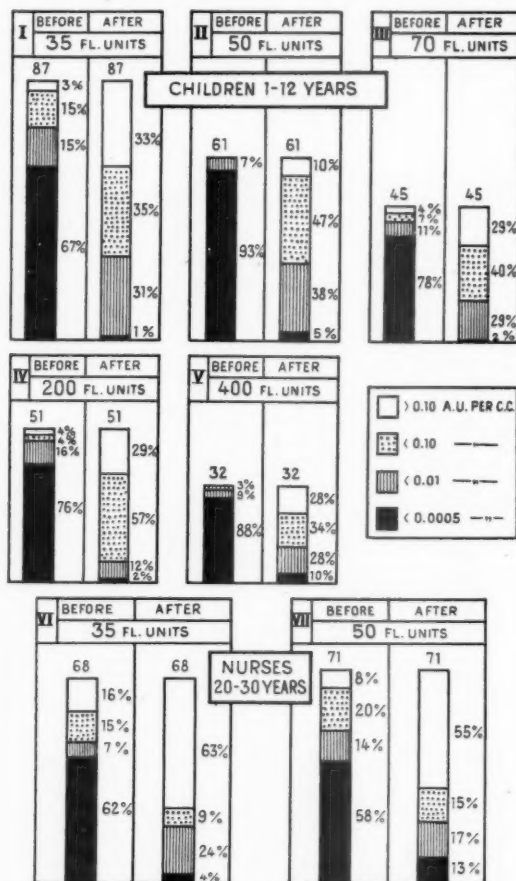


FIG. 5.—The antitoxin response in children and adults to a single injection of purified $Al(OH)_3$ -toxoid in increasing doses.

state of natural immunity to diphtheria at present in Denmark and may well be correlated with the low incidence of diphtheria in the last ten years demonstrated in Table I. This low natural immunity in Denmark is regarded as of serious importance and a commission of health authorities has recently been appointed, with the Director of the National Health Service for Denmark, Dr. Johs. Frandsen,

as president, with the object of starting a campaign for mass-immunization in order to close the stable door before the horse, "malignant diphtheria", has bolted.

If we now consider the response to the single subcutaneous injection, it should be emphasized that, irrespective of the dose given, even in the children with no natural antitoxin a detectable production of antitoxin occurs in about 95%. This is a typical response to the stimulus provided by the preparation we have used and indicates that it must be regarded as a very potent antigen.

If considered in relation to the doses of the antigen preparation, it is clear that the larger doses do not result in a conspicuous improvement in the effect.

We have not given smaller doses than 35 fl. units in children. On the whole, a dose of antigen of 1 c.c. = 35 to 50 fl. units + 10 vol.% Al(OH)₃ seems to give practically a maximum response. In any case, the improvement obtained by increasing the dose is not so marked or so constant as to lead us to recommend that larger doses should be given. In this connexion the question of expense, and especially that of the increasing local and general reactions, as will be seen later, have to be considered.

TABLE I.

YEAR	TOTAL CASES	ATTACK-RATES PER 1,000 POPULATION	TOTAL DEATHS	DEATH-RATES PER 10,000 POPULATION	CASE MORTALITY PER CENT
(1)	(2)	(3)	(4)	(5)	(6)
AVERAGE 1921-1925	7581	2.26	281	0.84	3.7
1926	5315	1.54	154	0.45	2.9
1927	5057	1.46	159	0.46	3.1
1928	5752	1.64	190	0.54	3.2
1929	4699	1.34	119	0.34	2.5
1930	5416	1.53	147	0.42	2.7
1931	3598	1.01	116	0.33	3.2
1932	3037	0.85	75	0.21	2.5
1933	2118	0.58	61	0.17	2.9
1934	2155	0.59	67	0.18	3.1
1935	3807	1.03	165	0.45	4.3
1936	2149	0.58			

Diphtheria incidence and mortality in Denmark, 1921 to 1936.

The antitoxin response to a single injection of alum-toxoid.—As alum-toxoid is now used rather extensively in other countries, it was of interest to compare the effect of a single subcutaneous dose of this preparation with the effect obtained with our purified aluminium-hydroxide toxoid.

Through the courtesy of a foreign institute we have obtained samples of an alum-toxoid preparation, which had been used extensively with good results in children. In collaboration with Dr. Bojlén, we have been able to test the antitoxin response to a single dose of this antigen in a group of 22 children, four and ten weeks after the injection (Table II).

It will be noticed from column 4 that the effect is very poor, as only two of the children, who had no antitoxin before the inoculation, show more than 0.01 unit. Ten weeks after (column 5) there is some improvement, especially in the poorer responders.

But when we compare the effect, as judged by the respective natural and artificial antitoxin spectra, with the results obtained in similar groups of children with purified Al(OH)₃-toxoid, the difference is striking and leaves no doubt that this alum-toxoid preparation in the dose recommended is a poorer antigen.

TABLE II

ALUM-TOXOID: 1 c.c. = 20 FL. UNITS + 33 VOL.% ALUM s.c.				
SERI- AL	AGE IN YEARS	ANTITOXIN UNITS PER C.C. SERUM		
		BEFORE	4 WEEKS AFTER	10 WEEKS AFTER
		THE SINGLE INJECTION		
NO.	NO.	NOV. 3rd, 1936	DEC. 1st, 1936	JAN. 13th, 1937
(1)	(2)	(3)	(4)	(5)
1427	6	} <0.0005	0.035	0.0125
1415	7		0.035	0.005
1408	7		0.008	0.01
1426	4		0.0015	0.0015
1412	7		0.0012	0.0024
1421	5		0.001	0.004
1402	6		0.001	no sample
1422	5		0.0008	0.005
1414	7		0.0008	0.00125
1405	7		0.0008	0.0011
1420	6		0.00075	0.019
1423	4		0.0007	0.001
1407	7		0.00065	0.0064
1404	7		0.0006	no sample
1413	7		0.00055	0.001
1424	5		0.00055	0.001
1428	6		<0.0005	0.0022
1406	9		<0.0005	0.0011
1409	7	<0.0005	<0.0005	
1416	7	<0.0005	<0.0005	
1425	5	0.0035	2.2	0.75
1417	7	0.003	0.2	0.2

The antitoxin response in children to a single subcutaneous dose of alum-toxoid four and ten weeks after the injection.

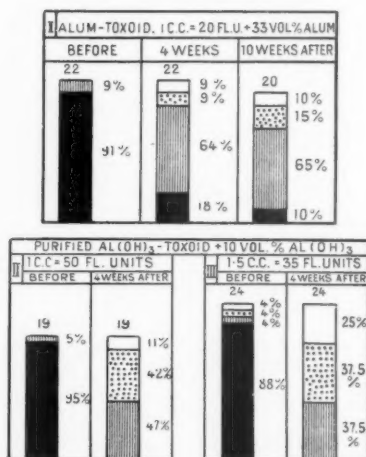


FIG. 6.—Comparison between the antitoxin response to a single subcutaneous dose of alum-toxoid and purified $\text{Al}(\text{OH})_3$ -toxoid in children.

The local and general reactions to a single injection of purified $Al(OH)_3$ -toxoid.—The reactions observed may be dealt with quite briefly. When ordinary crude toxoids are injected, the local and general reactions observed are partly due to the unspecific constituents (proteins, salts, &c.) and partly to the specific antigen.

The more pronounced local and general reactions are due to a hypersensitiveness to the specific antigen in the individuals inoculated, as shown very clearly in the previously mentioned group of children in Mattersburg, Austria, in the age-group 2 to 11 years. 123 of these had previously had diphtheria, while the rest had no history of diphtheria. It will be noticed that in the former group the reactions are more than twice as frequent as in the latter group.

For this reason the injection of even the very highly purified antigen preparations which we have used will give some reactions, but naturally they will be less frequent and much less pronounced than those provoked by equivalent antigen quantities of crude toxoids, as the local and general reactions caused by the unspecific constituents of these do not occur.

TABLE III.

TYPE OF REACTION	123 CHILDREN (2-11 YEARS) WHO PREVIOUSLY HAD DIPHTHERIA			430 CHILDREN (2-11 YEARS) WITH NO HISTORY OF DIPHTHERIA		
	NO.	PER CENT	STANDARD DEVIATION	NO.	PER CENT	STANDARD DEVIATION
(1)	(2)	(3)	(4)	(5)	(6)	(7)
SWELLING	3	2.4	1.39	6	1.4	0.57
SWELLING & REDNESS	24	19.5	3.58	38	8.8	1.37
TEMPERATURE ABOVE 38° C.	16	13.0	3.03	25	5.8	1.12
TOTAL REACTIONS	43	35.0	4.3	69	16.0	1.78

Reactions of 123 children who had had diphtheria, and 430 children with no previous history of diphtheria, to a single subcutaneous injection of purified $Al(OH)_3$ -toxoid. Dose: 2 c.c. = 50 fl. units + 10 vol. % $Al(OH)_3$.

We have been able to study the reactions to a single injection of purified $Al(OH)_3$ -toxoid in a number of children at various institutions, hospitals, &c.

Table IV gives the reactions to a medium dose of purified $Al(OH)_3$ -toxoid (i.e. 1.5 c.c. = 35-50 fl. units) in 307 children from 2 to 15 years old. In this and the following tables, we have distinguished between three degrees of reactions, indicated at the bottom of the table. It will be noticed that the number of reactions caused by purified toxoid increases with the age of the children—just as found for ordinary toxoid. In children below the age of 7 years, not less than 82% show no reactions at all, and if we discard the negligible first-degree reactions only 7% show moderate to strong local reactions with or without temperature. Of the children in the age-group 7 to 15 years, about 80% show no, or only negligible, reactions. In the majority of cases all reactions have disappeared after twenty-four hours, but in a few instances they may persist for forty-eight hours. In no case have the reactions been "serious" or "alarming" and no sequelæ have been observed, especially no abscess-formation.

It is of interest to compare these reactions with those observed after a single subcutaneous injection of the alum-toxoid preparation just mentioned. It will be

TABLE IV.

PURIFIED $Al(OH)_3$ -TOXOID. DOSE: 1.5 c.c. = 35-50 FL. UNITS + 10 VOL. % $Al(OH)_3$									
TYPE OF REACTION ^{a)}	72 CHILDREN 2 - 7 YEARS			235 CHILDREN 7 - 15 YEARS			TOTAL: 307 CHILDREN 2 - 15 YEARS		
	NO.	PER CENT	STANDARD DEVIATION	NO.	PER CENT	STANDARD DEVIATION	NO.	PER CENT	STANDARD DEVIATION
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
1st DEGREE	8	<u>11.1</u>	3.71	21	<u>8.9</u>	1.86	29	<u>9.4</u>	1.67
2nd -	2	<u>2.8</u>	1.94	35	<u>14.9</u>	2.31	37	<u>12.1</u>	1.86
3rd -	3	<u>4.2</u>	2.36	15	<u>6.4</u>	1.60	18	<u>5.9</u>	1.35
TOTAL: 2nd & 3rd DEGREE	5	<u>6.9</u>	3.00	50	<u>21.3</u>	2.68	55	<u>17.9</u>	2.20
ALUM - TOXOID. DOSE: 1 c.c. = 20 FL. UNITS + 33 VOL. % ALUM PRECIPITATE									
	12 CHILDREN 4 - 7 YEARS			15 CHILDREN 7 - 9 YEARS			TOTAL: 27 CHILDREN 4 - 9 YEARS		
	NO.	PER CENT	STANDARD DEVIATION	NO.	PER CENT	STANDARD DEVIATION	NO.	PER CENT	STANDARD DEVIATION
1st DEGREE	3	<u>25</u>		3	<u>20</u>		6	<u>22</u>	
2nd -	3	<u>25</u>		2	<u>13</u>		5	<u>19</u>	
3rd -	1	<u>8</u>		5	<u>33</u>		6	<u>22</u>	
TOTAL: 2nd & 3rd DEGREE	4	<u>33</u>	13.6	7	<u>47</u>	12.9	11	<u>41</u>	9.45
^{a)} 1st DEGREE - LOCAL REACTION: SLIGHT SWELLING and for REDNESS, LESS THAN 2-3 cm in DIAMETRE. 2nd - - LOCAL REACTION: MEDIUM TO STRONG SWELLING and REDNESS, 5-10 cm in DIAMETRE. 3rd - - GENERAL REACTION (ESPECIALLY TEMP. ABOVE 38°C) ACCOMPANIED BY LOCAL REACTION OF 1st or 2nd DEGREE.									

Reactions to a medium dose of purified $Al(OH)_3$ -toxoid in 307 children from 2 to 15 years of age in comparison with a single injection of alum-toxoid in 27 children from 4 to 9 years of age.

TABLE V.

PURIFIED Al(OH) ₃ -TOXOID				NUMBER OF INDIVIDUALS INOCULATED	AGE IN YEARS	DEGREE OF REACTION				
DOSE INJECTED						1st		2nd	3rd	2nd + 3rd
TOTAL VOLUME c.c.	FLOCC. UNITS	TOTAL N mg	Al - PRECI- PITATE (as Al ₂ O ₃) mg			NO.	PER CENT	NO.	NO.	PER CENT
(1)	(2)	(3)	(4)			(5)	(6)	(7)	(8)	(9)
1.5	<u>35</u>	0.10	2.6	183	2-15	17	9	17	10	<u>14.8</u>
0.5	<u>50</u>	0.15	0.85	88	2-15	10	11	17	7	<u>27.2</u>
1.5	<u>50</u>	0.15	2.6	43	2-12	5	12	7	6	<u>30.2</u>
<u>3.0</u>	<u>70</u>	0.20	<u>5.2</u>	31	7-15	7	<u>23</u>	15	1	<u>51.6</u>
2.0	<u>200</u>	0.60	3.4	63	2-11	9	14	20	11	<u>49.2</u>
2.0	<u>400</u>	1.2	3.4	30	2-13	4	13	9	14	<u>77.0</u>
1.0	<u>35</u>	0.10	1.7	221	20-30	96	43.4	54	41	<u>43.0</u>
ALUM - TOXOID										
1.0	<u>20</u>	1.0	<u>7.9</u>	27	4-9	6	<u>22</u>	5	6	<u>40.7</u>

Correlation between subcutaneous dose of antigen and frequency of reactions of second and third degree in children and adults.

noticed that although the dose contained only 20 fl. units, i.e. half the quantity of specific antigen employed above, the number of local and especially general reactions are significantly higher.

By comparing columns 2 and 11 in Table V, the close correlation between the dose injected and the percentage of reactions of second and third degree will be evident.

We may also point out that the reactions observed in 221 probationers in the age-group 20 to 30 years, as would be expected, are more numerous, pronounced and prolonged than in children. 25% show medium to strong local reactions and less than 20% general reactions (temperature, headache, nausea, fatigue, &c.). Also here there were no sequelæ and no cases of abscess-formation. In spite of these reactions, it has been possible to inoculate more than 400 nurses without trouble or mishap.

IMPROVEMENT OF THE "ONE-DOSE-IMMUNIZATION" METHOD

As demonstrated by the artificial antitoxin spectra given, a single injection of a medium dose of purified $\text{Al}(\text{OH})_3$ -toxoid in children results in antitoxin production in 90-99%, with a minimum of by-effects.

This procedure might therefore appear admirably suitable for mass-immunization since 80% or more would seem to be immune in four weeks. The demands made for methods of active immunization have, however, steadily increased, and it will be evident from what has been said above that I do not consider this method as quite satisfactory. The public, the doctors, and the health authorities want a method which will give immunity in 100% of cases, cause no reactions whatsoever, and be easy and cheap in administration. Although a biologist knows that this is more or less a Utopia, we must, however, endeavour to get as near to this ideal as possible.

It is for these reasons that I have tried to find a way of improving the effect of the single injection. The attempts to improve the effect by increasing the single dose were not very satisfactory. Some experiments in rabbits, with another object in mind, indicated that dilute purified toxoid administered intranasally was absorbed readily and acted as very potent secondary stimuli in rabbits previously inoculated.

"Rhino-vaccination" has formerly been tried by several workers (Dzierzgowsky, 1910, but especially Ramon and Zoeller, 1927a, b, c, and d, Salviolo, 1928, and others) with varying success but the general opinion is that the effect is too slow and too poor, even with prolonged administration of toxoid. Immunization by the nasal route alone is therefore not practicable.

The combination of the subcutaneous and intranasal routes of immunization has, however, not hitherto been carefully investigated.

As a single dose of Schmidt's purified $\text{Al}(\text{OH})_3$ -toxoid gives some basic immunity in almost 100% of cases it seemed promising to combine this effect by intranasal administration of purified toxoid.

In this way the natural process of immunization would be imitated, but in a greatly improved form. Contrary to the immunization by natural environmental stimuli (infection by *C. diphtheriæ*), the nasal immunization by toxoid is without any risk or by-effects, can be given in big doses, is not left to chance, and can be applied at the most opportune moment.

ACTIVE IMMUNIZATION BY THE COMBINED SUBCUTANEOUS AND INTRANASAL METHOD

I.—EXPERIMENTS ON RABBITS

To obtain some information as to the optimum conditions for nasal immunization in children a series of experiments on rabbits were undertaken. These were planned in such a way that parallel investigations could be made in children. The antigens were chosen so that identical preparations were used both on rabbits and in children, but the doses employed on rabbits were in most cases fixed at one-tenth of the doses intended for use in children.

A. The antigens used and their preparation.—Two different preparations were used, one for the subcutaneous injection and the other for the nasal instillation. In both preparations the active principle was highly purified and concentrated formol toxoid, the most essential difference being that the preparation for injection contained an admixture of 10 volumes % of the special $\text{Al}(\text{OH})_3$ -suspension, whereas the antigen preparation for nasal instillation was a clear isotonic, buffered (pH 7.3) dilution of highly purified formol toxoid, the application of which was made by slowly instilling five drops into each nostril.

B. The effect of varying the nasal doses and the intervals.—It will not be possible to give the details of the rabbit experiments; they will be published presently elsewhere, but Tables VI and VII, and a few curves showing the antitoxin response in rabbits

TABLE VI.

GROUP OF RABBITS & DATE OF INJECTION	SUB-CUTANEOUS DOSE	INTERVAL BETWEEN INJECTION & FIRST NASAL DOSE	INTRANASAL INSTILLATIONS																
			SINGLE NASAL DOSE (10 DROPS)	NUMBER OF DOSES	TOTAL NASAL DOSE	DISTRIBUTION OF INSTILLATIONS ON DAYS													
						1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	11th	12th	13th	14th
(1)	(2)	(3)	(4)	(5)	(6)	(8)													
I AUG. 24th 1933	Q.10 c.c. = 3.5 FL. Units + 10 Vol. AL(OH)3	4 WEEKS	2.5 FLU.	6	15	•	•	•	•	•	•	•	•	•	•	•	•	•	•
II AUG. 24th 1933		4 WEEKS	0.25 FLU.	6	1.5	•	•	•	•	•	•	•	•	•	•	•	•	•	•
III AUG. 24th 1933		4 WEEKS	2.5 FLU.	12	30	•	•	•	•	•	•	•	•	•	•	•	•	•	•
IV OCT. 18th 1933		2 WEEKS	2.5 FLU.	6	15	•	•	•	•	•	•	•	•	•	•	•	•	•	•
V SEPT. 10th 1935		4 WEEKS	2.5 FLU.	3	7.5	•	•	•	•	•	•	•	•	•	•	•	•	•	•

Doses of antigen, and intervals between doses, employed in the five groups of rabbits.

to the combined subcutaneous and intranasal method, will be sufficient for our purpose.

Fifty healthy white rabbits of uniform race and weight were divided into five groups of ten each.

All the rabbits received 3.5 fl. units of Schmidt's $\text{Al}(\text{OH})_3$ -toxoid subcutaneously. To study the effect of this and the subsequent nasal immunization a blood sample was taken from all the rabbits immediately before the first nasal instillations were given (i.e. four weeks after the subcutaneous injection with the exception of Group IV in which the interval was only two weeks) and a second blood sample six days after the last nasal dose.

The same procedure was followed in the investigations in children and adults.

Determination of the antitoxin titre of these first and second blood samples gives information as to the immunity response in the different groups to the subcutaneous and to the nasal immunization, respectively, at the times indicated.

When the last column in Table VII is studied, a positive correlation between the total nasal dose given and the increase, irrespective of the antitoxin level at four weeks, is obvious: Group IV shows a 55-fold increase, but this is not significantly higher than the 26- and 33-fold increase observed in Groups I and III (all three groups received the same total nasal dose, viz. 15 fl. units). Then follows Group V (total nasal dose 7.5 fl. units) with a 19-fold increase, and finally Group II, receiving only 1.5 fl. units intranasally, shows only an 8-fold increase.

TABLE VII.

GROUP OF RABBITS & DATE OF INJECTION	INTERVAL BETWEEN INJECTION & FIRST BLOOD-SAMPLE	ANTITOXIN UNITS PER C.C. AFTER INJECTION			INTERVAL BETWEEN INJECTION & SECOND BLOOD-SAMPLE	ANTITOXIN UNITS PER C.C. 1 WEEK AFTER NASAL INSTILLATIONS			INCREASE IN MEAN ANTITOXIN PRODUCED BY NASAL IMMUNISATION
		GEOMETRIC MEAN	LOG. GEO. MEAN	STANDARD DEVIATION		GEOMETRIC MEAN	LOG. GEO. MEAN	STANDARD DEVIATION	
I AUG. 24th 1933	4 WEEKS (SEPT. 20th)	0.248	1.395	0.480	6½ WEEKS (OCT. 7th)	6.55	0.816	0.389	26-FOLD
II AUG. 24th 1933	4 WEEKS (SEPT. 20th)	0.213	1.328	0.433	6½ WEEKS (OCT. 7th)	1.68	0.225	0.592	8-FOLD
III AUG. 24th 1933	4 WEEKS (SEPT. 20th)	0.199	1.298	0.433	6½ WEEKS (OCT. 7th)	6.65	0.823	0.425	33-FOLD
IV OCT. 18th 1933	2 WEEKS (OCT. 31th)	0.0483	2.684	0.304	4½ WEEKS (NOV. 11th)	2.67	0.427	0.420	55 FOLD
V SEPT. 10th 1935	4 WEEKS (OCT. 8th)	0.0631	2.800	0.426	6½ WEEKS (OCT. 29th)	1.22	0.086	0.399	19 FOLD

The antitoxin response in the five groups of rabbits as expressed by the geometric mean titre and the increase caused by the nasal instillations.

C. The antitoxin curve during combined subcutaneous and intranasal immunization in rabbits.—To get some detailed information concerning the effect of each nasal dose and the influence of varying the intervals between the doses, the antitoxin production in two rabbits in each group was followed closely in serial blood samples. Based on the antitoxin-response to the single subcutaneous injection, these two rabbits were selected in such a manner that one of them represented a poor and the other one a good antitoxin producer.

The results of the titration of the serial samples from the two rabbits selected from each group are given graphically in figs. 7 to 11.

Fig. 7 shows the typical secondary response to the nasal instillations of purified formol toxoid in the two rabbits selected from Group I.

In rabbit 2050 which had responded well to the subcutaneous injection, a rapid

rise in the antitoxin content occurs, with a maximum on the tenth day. After this the usual regular fall sets in.

It should be emphasized that the nasal instillations in the poor responder have been able to give an effect of the same order as in the good responder; furthermore, the right part of the curve indicates that the *durability of the immunity* (see Claus Jensen, 1933*a* and Dudley, 1934) induced in the poor responder is also not inferior to that produced in the good responder.

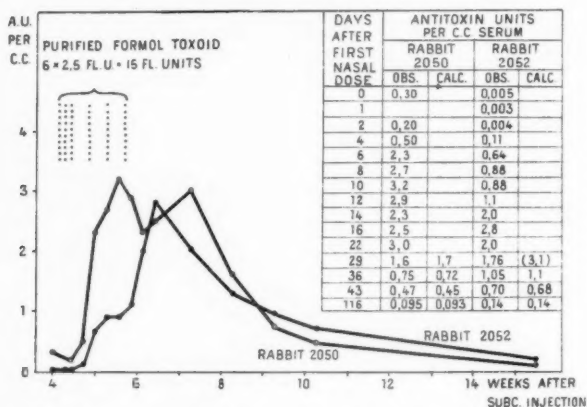


FIG. 7.—The response to nasal instillations in the two rabbits selected from Group I.

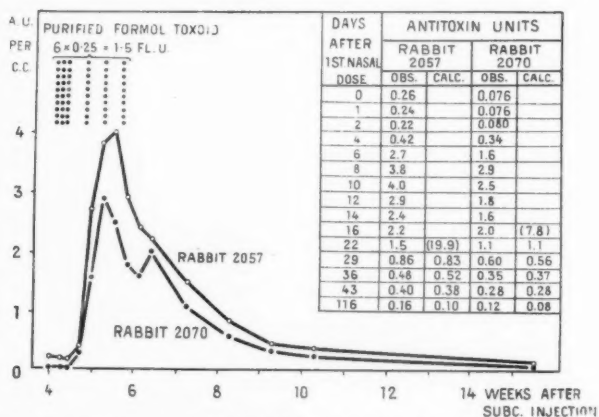


FIG. 8.—The response to nasal instillations ($\frac{1}{10}$ th of the dose used in Group I) in the two rabbits selected from Group II.

Fig. 8 gives the results obtained in the two rabbits selected from Group II. In this group all 10 rabbits responded rather well to the subcutaneous injection, and it has only been possible to study in detail the response in two rather good producers. Although the nasal doses employed in this group were only one-tenth of those used in the former group, a typical secondary response was obtained.

The response to *daily* nasal instillations in the good and poor producer selected from Group III is given in fig. 9.

In both cases an almost continuous rise is noticed during the whole period of treatment, but otherwise the daily nasal dosage has not given a better response.

In antidiphtheria campaigns, intervals longer than a fortnight are generally said to increase administrative difficulties. It was therefore of practical value to investigate whether a good response to nasal instillations could be obtained when the interval between the subcutaneous injection and the first nasal dose was shortened to two weeks instead of four weeks.

From the curves obtained in the two selected rabbits (fig. 10) it may be concluded that the shortening of the interval to two weeks has not prevented the nasal instillations from acting as potent secondary stimuli.

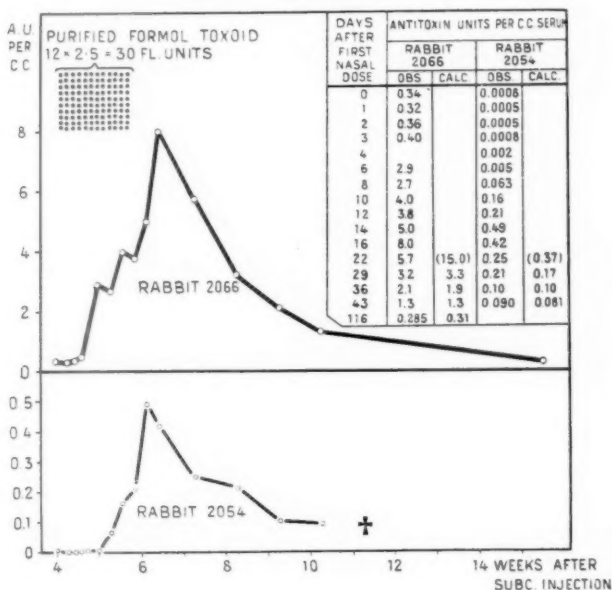


FIG. 9.—The response to *daily* nasal instillations in the two rabbits selected from Group III.

In the antitoxin curves demonstrated some of the nasal doses given seem to have had little or no effect. This indicated that it might be possible to obtain as good results with fewer nasal doses, which would simplify the procedure in its practical application to human beings.

In the fifth group of rabbits the number of nasal doses was therefore reduced from six to three, given at weekly intervals.

In fig. 11 the effect observed in three selected rabbits is given. Two of these rabbits had responded poorly, and the third well, to the subcutaneous injection.

The curves do not differ significantly from those obtained when six nasal doses are given. In most cases a rapid formation of antitoxin occurs, and the maximum is generally reached a few days after the last nasal dose.

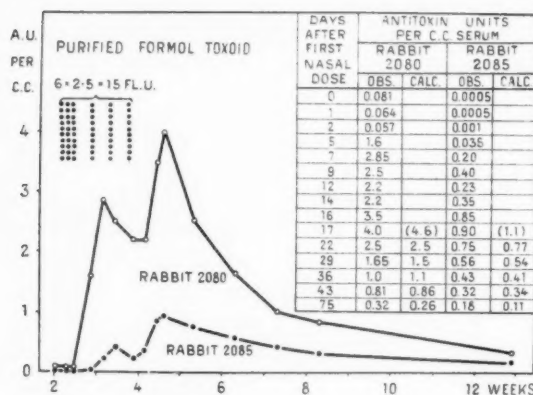


FIG. 10.—The response to nasal instillations given two weeks after the subcutaneous antigen injection in the two rabbits selected from Group IV.

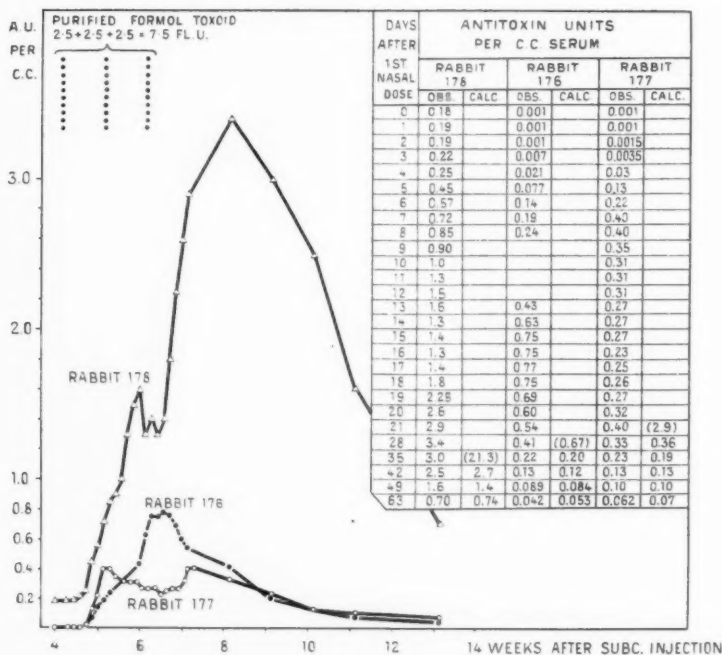


FIG. 11.—The response to three nasal instillations at weekly intervals in the three rabbits selected from Group V.

II.—INVESTIGATIONS IN CHILDREN AND ADULTS

Active immunization of children.—The first studies of the combined subcutaneous and intranasal method of immunization were undertaken at the Royal Institute for Deaf and Dumb Children in Copenhagen in 1933, in collaboration with Drs. Sv. Ahrend Larsen and Erin Madsen, and in Table VIII the details of the investigation are

TABLE VIII.

SERIAL NO.	AGE IN YEARS	ANTITOXIN UNITS PER C.C. SERUM		
		BEFORE THE SUBCUTANEOUS INJECTION ^{a)}	4 WEEKS AFTER	1 WEEK AFTER
		AUG. 3rd, 1933	SEPT. 19th, 1933	NASAL INSTILLATION ^{b)} OCT. 6th, 1933
(1)	(2)	(3)	(4)	(5)
2	6	<0.00005	0.40	
3	8		0.22	0.64
4	7		0.18	0.60
5	8		0.18	1.25
6	7		0.18	7.0
7	5		0.09	0.24
8	8		0.09	0.80
9	7		0.065	0.50
10	5		0.060	0.68
11	8		0.040	0.12
12	5		0.036	0.75
13	8		0.022	0.34
14	8		0.022	0.32
15	8		0.020	0.24
16	8		0.020	0.34
17	7		0.013	0.50
19	8		0.010	0.18
20	8		0.008	0.88
21	5		0.008	0.54
22	8		0.007	0.57
26	7		0.0045	0.34
27	5		0.0038	0.24
28	5		0.0018	0.54
1	7	0.0009	2.5	7.0
18	8	0.0007	0.0125	0.54
23	8	0.0007	0.0065	0.56
24	5	0.0008	0.005	0.54
25	7	0.0007	0.0045	
29	8	0.0008	0.0009	0.85
30	7	0.0125	15.5	14.5
31	7	0.067	7.0	7.0
32	6	0.017	7.0	7.0
33	8	0.0045	7.0	4.0
34	7	0.0038	0.48	1.8
35	7	0.25	0.40	50.0
36	8	0.20	0.20	12.5
37	8	0.060	0.16	6.5
38	6	0.064	0.11	6.0
39	7	0.030	0.065	7.5
40	8	0.040	0.050	16.0
41	8	0.0125	0.043	2.5
42	8	0.034	0.039	36.0

^{a)} PURIFIED $\text{Al}(\text{OH})_3$ -TOXOID. DOSE: 1.5 c.c. = 35 FL. UNITS + 10 VOL. % $\text{Al}(\text{OH})_3$
^{b)} PURIFIED DILUTE TOXOID. 6 DOSES; EACH DOSE = 10 DROPS = 25 FL. UNITS on SEPT. 19th, 20th, 21st, 24th, 27th and 30th.

The antitoxin response to the combined subcutaneous and intranasal immunization in 42 children from the Royal Institute for Deaf and Dumb Children in Copenhagen.

summarized. All the children received 1.5 c.c., corresponding to 35 fl. units of $\text{Al}(\text{OH})_3$ -toxoid, and four weeks after the injection the nasal instillations were given. The six doses, each corresponding to 25 fl. units, were distributed over a period of twelve days as in the rabbit experiments.

According to the antitoxin-titre of the primary blood samples, the children have been divided into three groups, the first group containing no detectable antitoxin, the second group containing traces of antitoxin, and the third group containing 0.01 unit or more. In the last group, most of the children respond well to the subcutaneous injection and also respond exceedingly well to the nasal instillations.

The results in the other two groups of children are, however, more important. First, it is to be noted that all the children show antitoxin production after the single subcutaneous injection. According to the titres observed four weeks after the injection, the children may be divided into two groups, a larger group with more than 0.01 unit and a smaller group showing less than this amount. The result in this latter group may be considered unsatisfactory. It will be noticed that this group

TABLE IX.

SERI- AL NO.	AGE IN YEARS	ANTITOXIN UNITS PER C.C. SERUM		
		BEFORE THE SUBCUTANEOUS INJECTION ^{a)}	4 WEEKS AFTER ^{a)}	1 WEEK AFTER NASAL INSTILLATION ^{a)}
		DEC. 16th, 1935	JAN. 9th, 1936	JAN. 30th, 1936
(1)	(2)	(3)	(4)	(5)
213	9	<0.0005	0.003	0.80
207	9		0.003	0.18
201	7		0.002	0.05
205	7		0.002	0.36
208	7		0.002	0.85
217	9		0.002	0.32
218	9		0.002	0.65
209	12		0.0018	0.36
210	7		0.0015	0.10
241	6		0.0009	0.25
244	6		0.0008	0.34
203	9		0.0008	0.25
211	8		0.0005	0.05
219	9		<0.0005	0.17
230	7		<0.0005	0.13
216	9		<0.0005	0.10
238	5	0.0008	0.002	0.64
245	7	0.0025	2.7	10.0
221	7	0.0025	0.15	0.13

^{a)} PURIFIED $\text{Al}(\text{OH})_3$ -TOXOID. DOSE: 1.5 c.c.-50 FL. UNITS + 10 VOL. % $\text{Al}(\text{OH})_3$

^{a)} PURIFIED DILUTE-TOXOID. 3 DOSES; EACH DOSE = 10 DROPS = 25 FL. UNITS on JAN. 30th, FEBR. 6th and 13th.

The antitoxin response to three nasal instillations in 16 children who had responded poorly to the subcutaneous injection

also responds very well to the nasal instillations. We have therefore *succeeded in transforming the poor responders into good ones*, and the immunity of the group of children as a whole after nasal instillations must be considered high.

Two years later another investigation in 42 children aged from 5 to 12 years was undertaken in the same institution in collaboration with Dr. K. Bojlén. A dose of 1.5 c.c., corresponding to 50 fl. units of purified $\text{Al}(\text{OH})_3$ -toxoid, was employed for the subcutaneous injection, and four weeks later the nasal instillations were given, but in this case only three doses with one week's interval.

Of the 42 children 39 had no natural antitoxin, and of these 16 responded poorly to the subcutaneous injection. The details of these 16 children may be studied in

Table IX. Of the total group all except two possess more than 0.10 unit one week after the instillations.

Practically the same dosage was used in a group of 20 children, the majority being between $\frac{1}{2}$ and 2 years of age. It is a well-known fact that small children are more difficult to immunize. It was therefore interesting to see whether good results would also be obtained by the combined method here. The results are given in Table X. It will be noticed that only one of the children had a small amount of natural antitoxin. The response to the subcutaneous injection is distinctly poorer than in the former groups. Nevertheless the nasal instillations give a very satisfactory secondary

TABLE X.

SERIAL NO.	AGE IN YEARS	ANTITOXIN UNITS PER C.C. SERUM		
		BEFORE THE SUBCUTANEOUS INJECTION	4 WEEKS AFTER ^{a)}	1 WEEK AFTER ^{a)} NASAL INSTILLATION
		DEC. 12th, 1935	JAN. 10th, 1936	JAN. 31st, 1936
(1)	(2)	(3)	(4)	(5)
318	5	<0.0005	0.10	1.0
321	1		0.04	0.35
302	$\frac{3}{4}$		0.035	0.30
310	2		0.03	0.50
314	2		0.02	0.37
304	$\frac{3}{4}$		0.015	0.32
308	1 $\frac{1}{2}$		0.015	0.60
311	2		0.015	0.70
313	2		0.015	0.65
301	$\frac{3}{4}$		0.0045	0.38
303	$\frac{3}{4}$		0.0045	0.38
306	1		0.004	0.38
309	1 $\frac{1}{2}$		0.003	0.24
317	4		0.003	0.38
315	4		0.0025	0.19
316	4		0.002	0.36
320	5		0.002	0.04
305	1		0.0015	0.68
312	2		0.002	
319	5	0.004	5.4	2.7

^{a)} PURIFIED Al(OH)_3 -TOXOID. DOSE: 1 c.c. = 50 FL. UNITS + 10 VOL. Al(OH)_3
^{b)} PURIFIED DILUTE-TOXOID. 3 DOSES: EACH DOSE = 10 DROPS = 25 FL. UNITS on JAN. 10th, 17th and 24th.

The effect of the combined method in twenty children from the Welander Home for Children, the majority $\frac{1}{2}$ to 2 years of age.

response even in the poor responders. Only one child has less than 0.10 unit and the rest have, as usual, $\frac{1}{4}$ to $\frac{1}{2}$ of a unit or more.

Table XI gives the results obtained in collaboration with the district health officer, Dr. A. Nielsen, at a home for boys, where some cases of diphtheria had occurred previous to the immunization. Thirty boys, in the age-group 9 to 15 years, were immunized by the combined subcutaneous and intranasal method. In this group no blood sample was obtained four weeks after the injection. The boys with natural antitoxin show, as would be expected, high titres after combined immunization, but the group without natural antitoxin also shows very satisfactory results, the minimum being 0.15 unit and the majority of the rest more than one full unit per c.c.

A summary of the results obtained by the combined method in the above four groups of children is given by the natural and artificial antitoxin spectra in fig. 12.

The first two groups received 6×25 fl. units intranasally and the artificial antitoxin spectra obtained one week later show that all 70 children have more than 0.10 unit.

The last two groups show much poorer natural antitoxin-spectra and received only 3×25 fl. units intranasally. In spite of this the final result one week after the last nasal dose is practically identical with that obtained in the two former groups.

TABLE XI.

SERI- AL NO.	AGE IN YEARS	ANTITOXIN UNITS PER C.C. SERUM	
		BEFORE THE INJECTION ^{a)}	1 WEEK AFTER NASAL INSTILLATION ^{a)}
		DEC. 8th, 1934	JAN. 22nd, 1935
()	()	()	()
45	13	<0.0005	6.4
27	13		6.3
18	13		6.2
9	9		5.9
64	12		4.9
32	14		4.0
58	12		3.3
1	10		2.8
56	12		1.75
33	13		1.7
13	10		1.5
59	12		1.5
2	9		1.0
5	10		0.85
50	14		0.85
57	10		0.78
70	12		0.15
67	9	0.009	1.0
42	14	0.090	49.0
6	11	0.016	25.0
48	12	0.07	15.0
68	9	0.090	14.0
80	15	0.06	13.0
72	14	0.06	8.5
69	12	0.086	6.5
38	14	0.032	5.6
17	11	0.063	4.2
40	14	0.090	3.5
3	11	0.015	3.4
20	13	0.08	1.3

^{a)} PURIFIED Al(OH)_3 -TOXOID. DOSE: 0.5 c.c. = 50 FL. UNITS + 10 VOL. % Al(OH)_3

^{b)} PURIFIED DILUTE TOXOID. 6 DOSES; EACH DOSE = 10 DROPS = 25 FL. UNITS on JAN. 4th, 5th, 6th, 9th, 12th and 15th.

The response to the combined subcutaneous and intranasal immunization in 30 boys from Fuglebjerg, where diphtheria had been endemic just before the immunization.

Active immunization of adults.—Through the courtesy of Professor Bie of the Blegdam Hospital (the isolation hospital) of Copenhagen, and in collaboration with Dr. Preben Plum, I have been able to make some investigations on some 600 probationer nurses in the age-group 20 to 30 years. A detailed report will be published shortly and only a few of the results obtained will be mentioned here.

Since October 1929 active immunization of all entering probationers has been carried out at the Blegdam-Hospital on the initiative of Professor Bie (1930). Thanks to the generous collaboration of the nurses, it was possible to try three different methods of immunization:—

(1) Exclusive nasal immunization by repeated series of instillations of purified toxoid-dilution,

(2) Subcutaneous immunization by repeated injections of Schmidt's purified $\text{Al}(\text{OH})_3$ -toxoid (1 c.c. = 35 fl. units) in doses of 1.0, 0.5, 0.5, &c., with three weeks' interval between the injections, and

(3) Combined subcutaneous and intranasal immunization.

The procedure in the first investigations was as follows: If the primary blood sample showed a titre equal to or above 0.10 unit, the nurse was not immunized. All the other nurses were immunized, until a titre of at least 0.10 unit had been observed.

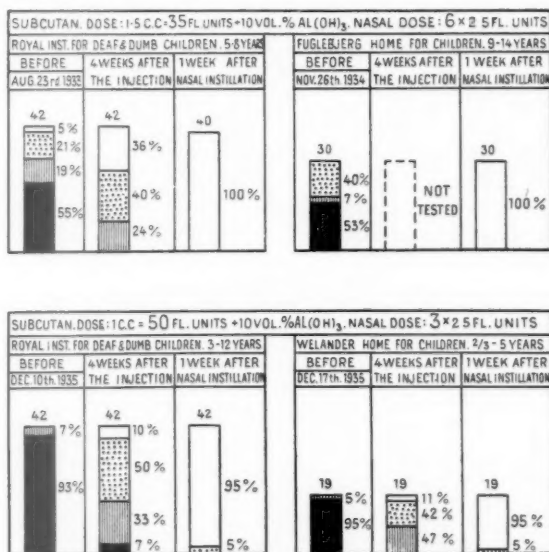


FIG. 12.—The response to immunization by the combined subcutaneous and intranasal method in four groups of children in Denmark.

In fig. 13 a summary of the effect of the two first methods of immunization is expressed by the natural and artificial antitoxin spectra. It is evident from the spectra of Group I that one series of nasal instillations caused only a very poor response and that the majority of nurses showed no antitoxin production. This is also true of the second and third series of instillations.

In the same way the spectra of Group II show that even after repeated injections of purified $\text{Al}(\text{OH})_3$ -toxoid, the antitoxin response was only mediocre. These methods therefore cannot be recommended.

The superiority of the combined subcutaneous and intranasal method of immunization is clearly illustrated (fig. 14) in a third group of nurses. One week after the last nasal dose, only 5% had a titre below 0.01 unit and 14% had between 0.01 and

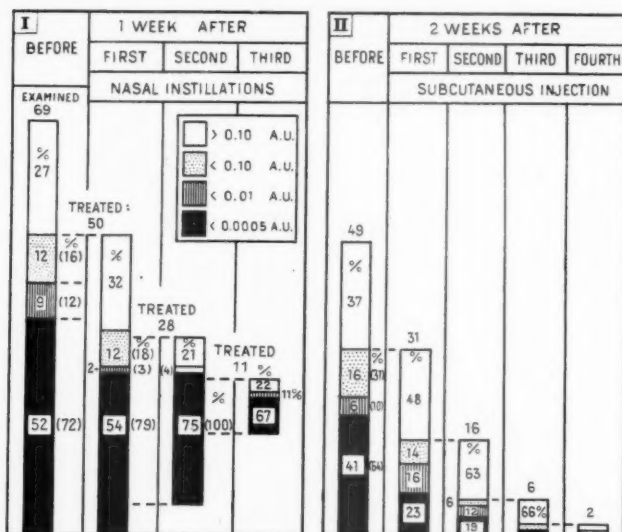


FIG. 13.—The antitoxin response in nurses to repeated nasal instillations of dilute toxoid and to repeated subcutaneous injections of purified $\text{Al}(\text{OH})_3$ -toxoid.

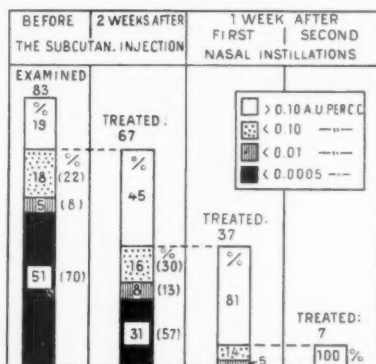


FIG. 14.—The antitoxin response in nurses to combined subcutaneous and intranasal immunization.

0.10 unit. A second series of nasal instillations was given to these seven poorer responders and a week later they all had more than 0.10 unit.

The combined method was now used on a larger scale at three hospitals in Copenhagen, as shown in fig. 15.

In Group I, the nasal dose employed was 6×25 fl. units and in Groups II and III 3×25 fl. units.

Fig. 16 shows the natural antitoxin spectrum of approximately 600 nurses in the age-group 20 to 30 years, before entering service at the Isolation Hospital. It is

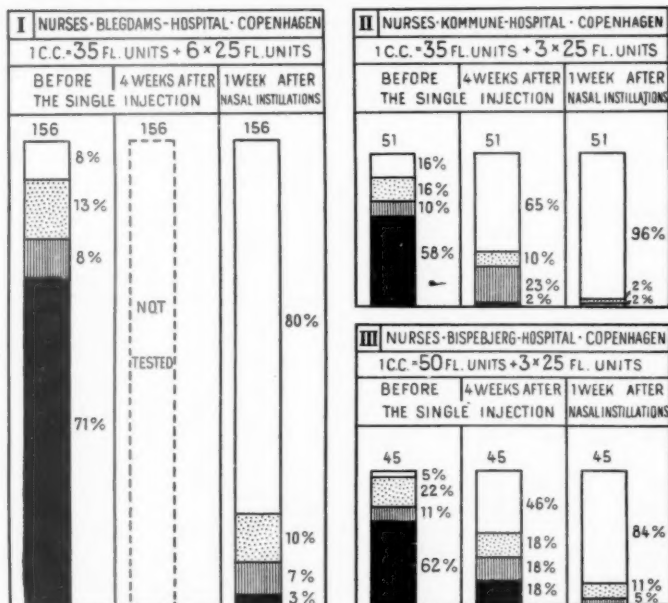


FIG. 15.—The antitoxin response in three groups of nurses to combined subcutaneous and intranasal immunization.

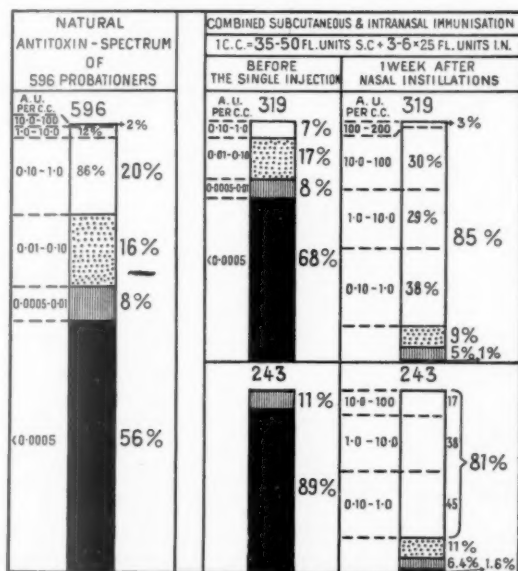


FIG. 16.—The natural antitoxin spectrum of 596 probationer nurses (from 20 to 30 years old) and the effect of combined subcutaneous and intranasal immunization on 319 of these.

noteworthy that not less than 64% had a titre below 0.01 unit and 56% had no detectable antitoxin. These high figures explain the rather numerous cases of diphtheria observed among the young probationers in the years before active immunization was adopted as a routine protective measure.

The response to the combined active immunization is given on the right. In all, 319 nurses have been treated with a subcutaneous injection of 35 to 50 fl. units, followed four weeks later by a series of from three to six nasal instillations, each nasal dose corresponding to 25 fl. units. The natural antitoxin-spectrum is a little poorer than in the total group, as individuals with a titre above 0.10 unit generally were excluded from treatment. 76% have less than 0.01 unit per c.c. and by far the majority of these possess no antitoxin. The response in these 243 individuals is given separately.

This group must be considered as a rather selected group of poor responders, as it consists of individuals who, even at an average age of 25 years, have not developed any circulating antitoxin. The artificial antitoxin-spectrum one week after the nasal instillations shows that only four individuals were refractory. Eight nurses showed small quantities of antitoxin and the rest, or 92%, had more than 0.01 unit. It should be noticed that the immunity of this latter group is very high, as 55% contain more than 1 unit and 17% of these have a titre between 10 and 100 units.

The investigations in nurses have shown that it is possible to obtain a very high group immunity by a single subcutaneous injection of purified $\text{Al}(\text{OH})_3$ -toxoid containing 35 fl. units and followed by three nasal instillations, each dose = 25 fl. units given four weeks later at weekly intervals.

This method of immunization has now been used at the Blegdam Hospital for more than two years as a routine protective measure, and has been made obligatory by Professor Bie for all probationer nurses before entering service at the hospital.

TABLE XII

Serial No.	Age in years	Antitoxin units per c.c. serum			
		Before the subcutaneous injection*	14 days after	1 week after first nasal instillations†	1 week after second nasal instillations†
(1)	(2)	(3)	(4)	(5)	(6)
62	27	< 0.0005	0.010	0.08	0.15
136	27		0.002	0.035	0.18
76	29		< 0.0005	0.085	0.30
114	28		< 0.0005	0.047	0.10
85	29		< 0.0005	0.045	0.66
111	26		< 0.0005	0.0035	0.19
109	30		< 0.0005	0.0008	0.13
316	22		Not tested	0.050	0.10
304	22			0.014	0.10
417	24			0.014	0.068
278	25			0.010	0.50
302	29			0.004	0.36
387	26			0.004	0.25
432	28			0.004	0.16
239	26			0.001	0.10
224	27			0.0009	0.002
245	25			0.0008	0.01
397	25	< 0.0005	< 0.0005	< 0.0005	0.05
405	26			< 0.0005	0.045

* Purified $\text{Al}(\text{OH})_3$ -toxoid. Dose: 1 c.c. = 35 fl. units + 10 vol.% $\text{Al}(\text{OH})_3$.

† Purified dilute toxoid. 6 doses (each dose = 10 drops = 25 fl. units) distributed over a period of twelve days.

The antitoxin response to a second series of nasal instillations in a selected group of 19 nurses, who had responded poorly to combined subcutaneous and intranasal immunization.

As already shown, the effect in the poorest responders may be increased considerably by a second series of nasal instillations. This is shown in Table XII, which contains a selected group of 19 nurses from the big group of 319 immunized by the combined method just mentioned. After the second series of nasal instillations,

only five contained less than 0.10 unit and only one of these less than 1/100th of a unit.

It may consequently be stated, that if *two* series of nasal instillations are used instead of one in the routine immunization of nurses by the combined method, an antitoxin titre of more than 0.10 unit will be obtained in 98.6% and more than 0.01 unit in 99.7% of cases.

THE PRACTICAL PREVENTION OF DIPHTHERIA BY THE COMBINED SUBCUTANEOUS AND INTRANASAL METHOD

The administration of the nasal instillations.—The remarks which follow are naturally based on the social and economic conditions we have in Denmark.



FIG. 17.—The nasal drops can easily be given by the child's mother.

In Great Britain it is possible that difficulties may be encountered in entrusting the nasal instillations to the mothers, especially in certain industrial centres where the home conditions are sometimes difficult for the proper and effective application of the method. In Denmark also difficulties may be encountered in certain districts, but it is considered that it should be quite possible by special arrangements to carry through the nasal immunization, for instance, through the district nurses or the welfare stations.

In institutions and schools, &c., practical administration of the nasal drops can easily be arranged collectively.

In the family in Denmark, the instillations in most cases can easily be given by the mother (fig. 17). A little instruction and the printed directions for use (*see Appendix*)

which should accompany the bottle of diphtheria prophylactic for nasal instillations, given to the mother when the child receives the subcutaneous injection, will be sufficient. Apart from a little tickling in the nose, *the nasal instillations of the highly purified, isotonic, and buffered toxoid-dilution do not give the slightest local or general reaction.*

Older children will therefore easily be persuaded to have the nasal drops, and to smaller children (below 2-3 years) and infants the nasal instillations can be given while they sleep.

The main objection to the introduction of the "combined" method in mass-immunization against diphtheria will no doubt be the uncertainty as to whether the children will be given the nasal instillations. Some health authorities may maintain that the bottle with the toxoid for nasal use is absolutely wasted, as the mothers will throw it away, considering it too difficult, or too much of a bother, to give the nasal instillations. Other field immunologists will, I hope, share my more optimistic views and have more reliance on the mothers. I am fully aware of the fact that it will require some enthusiasm and optimism in the field immunologist who really would like to apply the combined method in mass-immunization. But I am equally convinced that, by proper propaganda, the nasal instillations might easily enjoy a wide popularity as a simple and harmless means of reviving and prolonging the active immunity to diphtheria established by the single injection.

I would like here to refer to the excellent recent publication by Gundel (1936). By an elaborate and very detailed system of organization and propaganda he succeeded in getting on an average 90% of all children between 1 and 14 years of age, in some of the districts of the "Ruhrgebiet", inoculated by the *three (!)* injection method. During a few months more than 300,000 children were inoculated in this way. It should of course be emphasized that this result was obtained in a district at a time when the population, owing to recent diphtheria epidemics, was favourably inclined towards active immunization, and in a country where a number of special organizations co-operated. It is nevertheless an admirable example of how far a thorough propaganda and organization will help to immunize the total child population of a community.

The system of propaganda and organization employed by Gundel may easily be modified and adapted for use in other countries and will no doubt prove very valuable.

It has been stated that the immediate results of mass-inoculation against diphtheria may be very uncertain. The work of Gundel is the most recent and valuable contribution to the accumulated facts which eliminate any uncertainty as regards the immediate and ultimate beneficial effect of an energetically maintained effort.

Re-immunization by nasal instillations of purified toxoid.—As mentioned, the nasal instillations might well be used to advantage in the propaganda for an antidiphtheria campaign.

For example, it is easy to make the parents understand that the single injection protects most, but not all, children against diphtheria. By carefully administering the nasal drops according to the printed indications, the parent will co-operate with the doctor in fortifying and prolonging the protection very considerably, and thus reduce to a minimum the chance of their children contracting diphtheria. For the same reason it will be much easier to give a frank answer to the otherwise somewhat embarrassing question, very frequently put to the doctor by the child's mother: "How long will the protection last?" The obvious answer will be that this solely depends on her loyal co-operation.

This leads to the important question of routine and emergency re-immunization. The value of this procedure may be said to be generally recognized, but very little used. The "l'injection de rappel" recommended by the French authors (*see for*

example, Debré 1932), have for obvious reasons never been, and never will be, popular. The "fear of the needle" would, however, be avoided by substituting this injection by a few nasal instillations, which in this way might come to play a very important role as a safeguard against the "failures" which unfortunately still occur among actively inoculated individuals.

It was therefore of interest to study the effect of nasal instillations in children a considerable time after artificial immunization. In collaboration with Dr. Chas. N. Leach we have been able to follow the response to nasal re-immunization in two girls 7 and 9 years old respectively, who had been actively immunized six and seven years previously; in the case of Nancy with ordinary formol toxoid, while Caroline had received toxin-antitoxin mixtures.

As might be expected, the nasal instillations of toxoid act as very potent secondary stimuli (fig. 18).

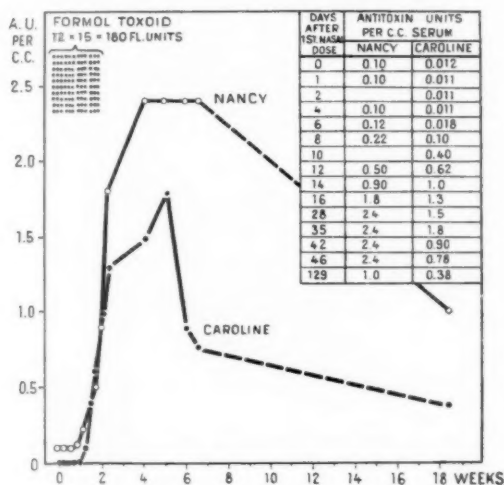


FIG. 18.—The response to nasal re-immunization in two girls, who had been actively immunized six and seven years previously.

In collaboration with Dr. Bojlén it has been possible to investigate the efficiency of the method of nasal re-instillation in a group of 23 children at the Royal Institute for the Deaf and Dumb in Copenhagen. As these children had been immunized about one year previously by the combined method, they also afforded a welcome opportunity of obtaining information as to the durability of immunity induced by this method of immunization.

In fig. 19 the natural and artificial antitoxin spectra observed in this group of children are given. Attention is drawn to the poor natural antitoxin spectrum which is much improved by the single injection, but especially by the first series of nasal instillations (column 3). Nine months later it was possible for us to test these children again, and the antitoxin spectrum showed that 39% now had less than 0.01 unit and resembled very much the one observed four weeks after the injection. A nasal re-immunization, however, gives a very marked improvement; 95% have now more than 0.10 and, of these, 62% have more than 1 unit.

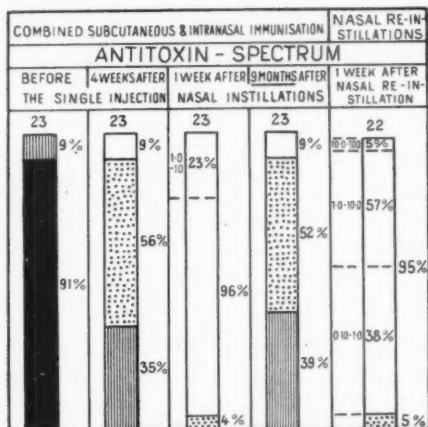


FIG. 19.—The natural and artificial antitoxin spectra of 23 children after combined subcutaneous and intranasal immunization and nasal re-immunization.

Some interesting details may be studied in Table XIII.

TABLE XIII.

SERI-	AGE	EFFECT OF COMBINED SUBCUTANEOUS AND NASAL IMMUNISATION				EFFECT OF NASAL RE-IN-STILLATION
		ANTITOXIN UNITS PER C.C. SERUM				
AL	IN	BEFORE	4 WEEKS AFTER	1 WEEK AFTER	9 MONTHS AFTER	1 WEEK AFTER
		THE SUBCUTANEOUS INJECTION ^{*)}	NASAL INSTILLATION ^{†)}	NASAL INSTILLATION ^{‡)}	NASAL INSTILLATION ^{§)}	NASAL RE-IN-STILLATION ^{¶)}
NO.	YEARS	DEC. 10th, 1935	JAN. 9th, 1936	JAN. 30th, 1936	NOV. 3rd, 1936	NOV. 24th, 1936
(1)	(2)	(3)	(4)	(5)	(6)	(7)
243	5		1.2	1.5	0.17	1.5
223	8		0.075	0.80	0.05	1.8
242	6		0.055	1.6	0.034	0.95
240	5		0.05	1.4	0.036	1.6
227	7		0.045	0.60	0.01	1.5
239	8		0.04	1.5	0.034	no sample
237	7		0.04	0.63	0.022	2.8
202	7		0.04	0.45	0.032	0.7
235	5		0.035	0.67	0.034	11.6
204	10		0.035	0.40	0.032	1.9
220	7	<0.0005	0.03	0.70	0.022	1.4
229	6		0.015	1.4	0.17	1.4
236	8		0.012	0.90	0.008	0.7
224	7		0.011	0.32	0.004	0.8
207	9		0.003	0.18	0.008	0.34
208	7		0.002	0.85	0.07	2.7
218	9		0.002	0.65	0.032	1.4
210	7		0.0015	0.10	0.0018	0.7
241	6		0.0009	0.25	0.008	1.5
244	6		0.0008	0.34	0.008	2.6
211	8		0.0005	0.05	0.0005	0.14
238	5	0.0008	0.002	0.64	0.004	0.85
221	7	0.0025	0.14	0.14	0.004	0.03

^{*)} PURIFIED A1(OH)₃-TOXOID. DOSE: 1.5 c.c. = 50 FL. UNITS + 10 VOL. % A1(OH)₃ s.c.

^{†)} PURIFIED DILUTE TOXOID. 3 DOSES; EACH DOSE = 10 DROPS = 25 FL. UNITS on JAN. 9th, 16th and 23rd.

^{‡)} PURIFIED DILUTE TOXOID. 3 DOSES; EACH DOSE = 10 DROPS = 25 FL. UNITS on NOV. 3rd, 10th and 17th.

The antitoxin response to nasal re-immunization in 23 children immunized approximately one year previously by the combined subcutaneous and intranasal method.

The titres found after the combined immunization are given in column 6 of the table. It will be noticed that seven of the nine children now showing an antitoxin titre below 0.01 are those who also responded poorly to the single injection. The children were now given three doses of purified toxoid intranasally. The nasal re-instillations cause a rapid and abundant production of antitoxin and, in the children containing less than 0.01 unit before the nasal re-instillations, the increase in most cases is 200 to 500-fold.

As shown, for example, by the investigations in nurses (see fig. 13, p. 92), immunization by the nasal route alone gives a poor response and should not be generally recommended.

It may, however, be of use in *especially exposed persons* above 15 years of age (for example, members of a household with a malignant case; hospital personnel in diphtheria wards, &c.) where the toxoid injection is contra-indicated or objected to. Individuals above this age frequently possess some basic immunity, and a few nasal instillations will therefore in many cases suffice to cause a very rapid increase in the circulating antitoxin.

TABLE XIV.

SERIAL NO.	AGE IN YEARS	ANTITOXIN UNITS PER C.C. SERUM		INCREASE IN 18 DAYS (APP.)
		BEFORE	1 WEEK AFTER NASAL INSTILLATION ^{a)}	
(1)	(2)	(3)	(4)	(5)
166	24	0.0006	5.6	10,000-FOLD
208	25	0.005	22.0	7,000 -
149	25	0.007	3.7	500 -
154	25	0.009	1.4	150 -
158	25	0.004	0.68	150 -
156	26	0.005	0.015	5 -
145	25	0.06	66.5	1,000 -
179	28	0.05	30.0	1,000 -
185	26	0.08	30.0	375 -
181	32	0.028	18.0	650 -
177	29	0.031	17.0	550 -
207	28	0.02	15.0	750 -
146	26	0.03	5.3	175 -
157	26	0.065	3.6	60 -

^{a)} DILUTE TOXOID. 6 DOSES (EACH DOSE = 10 DROPS = 15 FL. UNITS)
DISTRIBUTED OVER A PERIOD OF 12 DAYS.

Response to one series of nasal instillations (6 x 15 fl. units) in 14 nurses with some natural antitoxin.

This may well be of decisive significance in making highly exposed individuals able to resist an especially massive or malignant infection by virulent diphtheria bacilli.

Table XIV may serve as an example of this. Fourteen nurses, who had some natural antitoxin in the blood, were immunized intranasally as indicated at the bottom of the table, with very good results.

Advantages of the combined subcutaneous and intranasal method.—These may be summarized as follows:—

(1) Only a single injection is required. Consequently the child can only have one reaction, and, on account of the highly purified antigen and minimal quantity of aluminium hydroxide employed, these reactions are few in number, generally negligible and in no case "serious".

(2) On account of the depot-effect, the purified $\text{Al}(\text{OH})_3$ -toxoid acts as a series of stimuli. Even children and adults without any demonstrable basic immunity will therefore respond with antitoxin production in 90-99% of cases. By this "one-shot immunization", a comprehensive campaign may be carried out safely and easily.

The main objection to the exclusive use of this method is that too many cases of diphtheria might be notified amongst the only "partly" protected. This would

seriously affect the confidence of the population in the active immunization and the health authorities, which should be avoided. Any steps that might serve to reduce the occurrence of cases of diphtheria in so-called immunized individuals should be taken, regardless of possible expenditure and trouble.

It is for this reason that we strongly recommend the reinforcement and prolongation of the immunity by following up the response of the single injection with

(3) Three nasal instillations of purified toxoid in suitable doses and intervals, and further to revive and reinforce the immunity by

(4) Nasal re-immunization yearly in September, as a routine for children until the age of 7, and as an emergency for all previously immunized individuals at the onset of an epidemic.

Principles and dosage recommended.—For the subcutaneous injection purified $\text{Al}(\text{OH})_3$ -toxoid and for the nasal instillations purified toxoid in isotonic, buffered (pH 7.3) dilution should be used.

The principles to be followed and the dosage recommended may briefly be stated as follows:—

A. The Prophylaxis Proper.

(Prevention of diphtheria in non-epidemic periods.)

I. Children:

(1) *Under 6 months*: no active immunization; as an emergency *passive* immunization (see below, B, I (1)).

(2) *6 months to 14 years inclusive*: combined subcutaneous and intranasal immunization.

Dosage:	{	Subcutaneous dose: 1 c.c. = 50 fl. units + 10 vol.% $\text{Al}(\text{OH})_3$.
		Intranasal dose: 10 drops = 50 fl. units, 3 doses at weekly intervals.
		Nasal re-immunization: intranasal dosage as above. Repeated every year in September until the child is 7 years old.

II. *Adults*: (Individuals particularly exposed to infection, e.g. probationers, interns, and other hospital personnel before entering service in diphtheria wards, &c.) combined subcutaneous and intranasal immunization.

Dosage:	{	Subcutaneous dose: 1 c.c. = 25 fl. units + 10 vol.% $\text{Al}(\text{OH})_3$.
		Intranasal dose: As for children; if considered necessary 2 series.
		Nasal re-immunization: none.

B. Emergency Prophylaxis.

(Prophylaxis at outbreak of diphtheria epidemic.)

I. Individuals not inoculated previously:

(1) *Immediate* passive immunization of all possible contacts (members of households, institutions, schools, &c., where cases have occurred) by diphtheria antitoxin from goat or sheep.

Dosage:	{	Children up to 5 years: 500 A.U.	} intramuscularly
		Children up to 10 years: 1,000 A.U.	
		Older children and adults: 1,500 A.U.	

(2) *Simultaneous combined subcutaneous and intranasal immunization* according to the instructions given above (A, I) but with an interval of only two weeks between the single injection and first nasal dose.

(3) *Nasal immunization* of especially exposed children above 15 years and adults by nasal instillations: 6×25 fl. units during a period of twelve days.

II. Individuals immunized previously:

Immediate nasal re-immunization as above (A, I (2)) at all ages.

From our experiences in Denmark we are convinced that the combined subcutaneous and intranasal method will prove to be an effective and practicable means whereby the active immunization of human populations against diphtheria can be achieved.

I desire to point out, however, that the investigations recorded in this paper would not have been possible without the valuable assistance I have received from my collaborators Drs. *Sv. Ahrend Larsen, K. Bojlén, Preben Plum, Otto Kirstein, A. Nielsen, Erin Madsen, Johs. Ipsen*, and from my technical assistants, and many others; and especially to express my thanks to Dr. phil. *S. Schmidt* and *A. Hansen*, whose work on purified toxoid provided the basis for the combined subcutaneous and intranasal method of immunization which we have proposed.

APPENDIX.

Directions for Administration of Diphtheria Toxoid
for Nasal Immunization.

STATENS SERUM INSTITUT

Serum Department
Copenhagen, Denmark.

DIPHTHERIA PROPHYLACTIC (Diphtheria Toxoid) FOR NASAL INSTILLATION.

A single injection of the purified Diphtheria Prophylactic with aluminium hydroxide under the skin will render most children immune against diphtheria in a few weeks. Investigations have shown that this protection may be re-inforced and prolonged considerably when the children, four weeks after the injection, are given a few drops of Diphtheria Prophylactic into the nose.

For these nasal drops, a highly purified and diluted Diphtheria Prophylactic is used.

These instillations do not in any way trouble the children and may well be carried out by the child's mother. In order to obtain the desired effect it must be emphasized that the nasal drops should be given carefully according to the directions below.

DIRECTIONS FOR USE.

The child should lie down during the administration of the nasal drops, so that the Diphtheria Prophylactic instilled remains in the nose. The instillations are therefore most easily carried out in the morning before the child gets up, or in the evening when the child has gone to bed. Often the drops may successfully be given while the child is asleep. After each treatment, the child should remain lying for a couple of minutes.

NASAL DROPS ARE GIVEN IN THE FOLLOWING WAY:

The nose of the child must be blown carefully. After this, the point of the pipette (the glass-tube with the rubber-cap) is dipped into the Diphtheria Prophylactic and by compressing the rubber-cap for a moment, some of the dilution is sucked into the pipette. The point of the pipette is then placed over the nostrils and 5 drops are slowly instilled into each.

This treatment is given for the first time 4 weeks after the injection and repeated again one week and two weeks after, so that the child has received 3 instillations altogether.

In children below 6 years of age, it is strongly recommended that the nasal instillations are repeated every year in September and at the beginning of, or during, a diphtheria epidemic; this applies also to older children who have been previously immunized, and specially exposed adults, as the protection against diphtheria in this way will be re-inforced and prolonged.

REFERENCES

- BIE, V. (1930), *Ugesk. f. Laeger*, **92**, 635.
 DEBRÉ, R. (1932), "La vaccination contre la diphtérie", Paris.
 DUDLEY, SHELDON F., MAY, PERCIVAL M., O'FLYNN, JOSEPH S. (1934), "Active Immunization against Diphtheria", Medical Research Council, Special Report Series, No. 195.
 DZIERŻOŃSKY, S. K. (1910), *Z. Immun.-forsch.*, **2**, Ref. 602.
 FORBES, J. G. (1932), "Diphtheria Past and Present", London.
 GLENNY, A. T., SÜDMERSEN, H. J. (1921), *J. Hyg.*, **20**, 176.
 GLENNY, A. T., BUTTLE, G. A. H., STEVENS, F. (1931), *J. Path. and Bact.*, **34**, 267.
 GLENNY, A. T., WADDINGTON, H. (1929), *J. Path. and Bact.*, **32**, 275.
 GUNDEL, MAX (1936), "Die aktive Schutzimpfung gegen Diphtherie".
 Id. (1936), *Veröff. aus dem Geb. des Volksgesundheitsdienstes*, **67**, 387.
 JENSEN, CLAUD (1931), *Compt. rend. Soc. de biol.*, **108**, 528 and 532.
 Id. (1933a), *Acta path. et microbiol. Scandinav.*, **10**, 137.
 Id. (1933b), "Die intrakutane Kaninchenmethode zur Auswertung von Diphtherietoxin und Antitoxin", Copenhagen.
 LEACH, CHAS. N., JENSEN, CLAUD, PÜCH, G. (1935), *J. Lab. and Clin. Med.*, **20**, 451.
 Id. (1935), *Deutsche med. Wchnschr.*, **20**, 793.
 MONMIGNANT, F. (1927), *Thèse de Paris*, No. 372, p. 36.
 RAMON, G. (1923), *Compt. rend. Acad. d. sc.*, **177**, 1338.
 Id. (1931), *Ann. l'Inst. Pasteur*, **47**, 339.
 RAMON, G., NÉLIS, M. P. (1932), *C. R. Soc. Biol.*, **109**, 570.
 RAMON, G., ILLINGWORTH HELIE, M. G. (1928), *J.A.M.A.*, **91**, 1028.
 RAMON, G., ZOELLER, CHR., (1927a), *Compt. rend. Soc. de biol.*, **96**, 757.
 Id. (1927b), *ibid.*, 701.
 SALVIOLO, G. (1928), *Pediatrics*, **26**, 687.
 SCHMIDT, S., LINDERSTROM-LANG (1930), *Compt. rend. Soc. de biol.*, **102**, 618.
 SCHMIDT, S. (1931), *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, **71**, 101.
 Id. (1932), *Acta path. et microbiol. Scandinav.*, **9**, 269.
 SCHMIDT, S., HANSEN, A., KJÆR, K. A. (1931), *Ann. Inst. Pasteur*, **46**, 202.
 SCHMIDT, S., HANSEN, A. (1933), *Acta path. et microbiol. Scandinav.*, Suppl. **16**, 407.
 ZOELLER, CHR., RAMON, G. (1927c), *Bull. Acad. de méd., Paris*, **97**, No. 26.
 Id. (1927d), *Presse méd.*, **69**, 1049.

Section of Odontology

President—W. WARWICK JAMES, O.B.E., F.R.C.S., L.D.S.E.

[March 19, 1937]

Local and Remote Sequelæ of Infection in the Parodontal Sulcus

By E. WILFRED FISH, M.D., D.D.Sc., D.Sc.

(From the John Hampton Hale Research Laboratory, Royal Dental Hospital
and School of Dental Surgery, London)

ABSTRACT.—(1) It is shown in this paper that the infecting organisms in the parodontal sulcus are confined to the surface, but may be forced into the blood and lymph stream by traumatic interference.

2. Local and general disturbances may therefore arise both as a result of the absorption of soluble toxic matter from the pocket into the tissues and also as a result of this traumatic introduction of organisms into the blood-stream.

3. The effect of toxic absorption on the local tissues is destruction of the attachment of the tooth—pyorrhœa.

4. The remote effects of toxic absorption may be a similar destruction of the connective tissue generally—arthritis and fibrositis. The liver and kidney may suffer since they excrete the toxic matter, and other susceptible tissues may also be involved.

5. Traumatic bacteræmia may produce local bone necrosis or “dry” socket. Acute suppurative lymphangitis produces the “pyorrhœtic abscess”.

6. The remote effect of bacteræmia may be to produce osteomyelitis (e.g. of the tibia) or to convert a simple endocarditis into the bacterial type.

7. The mechanism of bone absorption and deposition in response to irritation is discussed.

8. Methods of eliminating parodontal infection are referred to and the importance of complete elimination is stressed. It is shown to be not incompatible with the conservation of the teeth.

RÉSUMÉ.—1. Il est démontré que l'agent infectieux dans le sulcus paradentaire est limité à sa surface, mais peut être introduit dans la circulation sanguine ou lymphatique par des interventions traumatiques.

2. Des troubles locaux ou généralisés peuvent donc survenir comme suite de l'absorption de toxines solubles dans la poche paradentaire ainsi que par l'introduction traumatique des germes dans la circulation sanguine.

3. L'effet local de l'absorption des toxines est la destruction de l'attache de la dent—la pyorrhée.

4. L'effet éloigné de l'absorption toxique peut être une destruction analogue du tissu conjonctif en général—arthrite et fibrosite. Le foie et le rein peuvent en souffrir, car c'est par eux que les toxines sont éliminées, et d'autres tissus susceptibles peuvent aussi être atteints.

5. La bactériémie traumatique peut produire une nécrose osseuse locale ou alvéole “sèche”. La lymphangite suppurée produit l’ “abcès pyorrhéal”.

6. L'effet éloigné de la bactériémie peut se manifester comme ostéomyélite, par exemple du tibia, ou transformer une endocardite simple en endocardite bactérielle.

7. Le mécanisme de l'absorption et de la déposition de tissu osseux comme réaction à l'irritation est discuté.

8. L'auteur parle des moyens d'éliminer l'infection paradentaire, faisant spécialement ressortir l'importance de l'élimination complète, qui n'est pas incompatible avec la conservation des dents.

ZUSAMMENFASSUNG: 1. In der vorliegenden Arbeit wird gezeigt, dass die die paradentale Tasche infizierenden Keime auf die Oberfläche begrenzt sind, jedoch durch traumatische Einflüsse in den Blut- und Lymphstrom hineingepresst werden können.

2. Oertliche sowie Allgemeinstörungen können daher sowohl durch Resorption von löslichem toxischem Material aus der Tasche in die Gewebe als auch infolge eben dieser traumatischen Einpressung von Organismen in den Blutstrom entstehen.

3. Der Einfluss der Giftresorption auf die lokalen Gewebe äussert sich in Zerstörung der Zahnbefestigung—Pyorrhoe.

4. Die Fernwirkung der Giftresorption kann in einer analogen Zerstörung des Bindegewebes im allgemeinen bestehen—Arthritis und Fibrositis. Da Leber und Nieren die toxischen Stoffe ausscheiden, können sowohl diese als auch andere empfindliche Organe ebenfalls in Mitleidenschaft gezogen werden.

5. Die traumatische Bakteriämie kann zu lokalen Knochennekrosen oder zu "trockener" Alveole führen. Eine akute eitrige Lymphangitis führt zum "pyorrhoeischen Abszess."

6. Durch Fernwirkung der Bakteriämie kann eine Osteomyelitis (z.B. der Tibia) entstehen oder eine einfache Endokarditis in die bakterielle Form übergeführt werden.

7. Der Mechanismus der Knochenresorption und -ablagerung, wie sie als Folge der Reizung auftreten, wird besprochen.

8. Methoden zur Beseitigung der paradentalen Infektion werden erwähnt und es wird die Bedeutung der restlosen Beseitigung betont. Es wird gezeigt, dass diese mit der Erhaltung der Zähne durchaus vereinbar ist.

INTRODUCTION

THE purpose of this paper is to review the immediate effect of the organisms which inhabit the periodontal sulcus on the surrounding tissues, and also to consider their remote effect on the general health.

The subject is approached mainly from the clinical aspect and is discussed in the light of recent findings which are firmly supported by experimental evidence. These have shown on the one hand that, when undisturbed, the bacteria remain localized to the surface in the chronic pyorrhœa pocket and only the toxic products of their activity are absorbed (Fish and Maclean [2]), whereas on the other hand any traumatic disturbance of the inflamed gum margin may drive the organisms into the blood-stream and produce a transient bacteraemia (Okell and Elliott [7]) and Round, Kirkpatrick, and Hails [8]). These observations only refer to chronic infections.

The discussion, therefore, deals with the effect of this absorption of toxic material both on the parodontal tissues and on the system generally, and is also extended to include the effect on both the local tissues and the more remote parts of the body when the infection itself is disturbed by trauma and actually gains access to the blood-stream or lymphatics.

The toxic material absorbed causes locally a breakdown of the parodontal tissues which is known as pyorrhœa, and upon general absorption produces various chronic disturbances of bodily function. The traumatic entry of organisms into the tissues produces acute septic inflammation either locally or at some distant point, but this only happens if they gain a foothold in a nidus of non-vital tissue. If they remain in the blood-stream they are soon eliminated quite harmlessly. The difference between acute and chronic inflammation when produced by the mouth streptococci is that in the former the organisms are violently introduced into the tissues and are being vigorously attacked by leucocytes, while in the latter they have been successfully confined to a necrotic nidus and the reaction in the surrounding tissues is due to the absorption of their toxic products [2].

LOCAL SEQUELÆ OF PARODONTAL INFECTION

Pyorrhœa, as its name to some extent suggests, is a chronic suppurative inflammation of the marginal tissues of the gum. In an established case it is characterized by a deepened periodontal sulcus, ulcerated, and lined with granulation tissue, on which a

degenerated epithelium grows either in sickly luxuriance, like a plant kept in a cellar, or wilts as a scanty remnant.

This condition, though almost universal in civilized communities, is neither healthy nor normal. Fig. 1, taken from the erupting molar of a rat, shows how the horny cuticle of the gum and that of the enamel (Nasmyth's membrane) are originally continuous and protect the living parodontal tissues beneath from injury by shooting the food over the streamline contour of the gum-enamel junction.



FIG. 1.—Photomicrograph ($\times 100$) of partly erupted molar tooth of rat, showing continuity of Nasmyth's membrane (N) and the horny cuticle of the gum (C). There is a keratinous invagination at K but no periodontal sulcus.

There is, however, as shown by Stewart-Ross, a dipping-in of the keratinized cuticle together with its supporting epithelium at the place where the remnant of the enamel organ (the epithelial attachment) joins the mouth epithelium. This arrangement gives a triple horny layer at the actual edge of the gum, and so provides for a rapid proliferation and keratinization of the epithelium at this all-important point where most of the masticatory stress falls. Unfortunately the device contains

within itself the germ of its own undoing, and so, like all Nature's biological experiments which inevitably end in death, it is, from the human point of view, a failure. This horny invagination tends to split and only friction by the roughest primitive food can prevent the periodontal sulcus from developing (fig. 1A).

There is a similar dipping-in of keratinized material at the base of the nail-bed, and even in the unmanicured monkey this keratinous invagination also shows some tendency to split (fig. 2). In over-manicured fingers, softened by disuse, chronic infection of the nail-bed, onychia, is not uncommon. The infection enters this crevice, and the nail may be loosened and lost like a tooth, only in such an event a new nail will grow.

Such easy replacement is, unfortunately, only an attribute of very simple structures. Observation of the primitive protozoa suggests a conception of life akin to immortality. The amœba rises revived like the Phoenix and duplicated at each translation. As soon, however, as specialization and cell-differentiation appear, somatic death becomes the rule and only the reproductive cells preserve this heritage of immortality. The price of individuality is death, and this principle applies to the teeth. The undifferentiated teeth of the shark persist in an endless series, but the human tooth is too specialized to be reproduced so freely, and though well adapted to its native purpose, it cannot survive the changed environment imposed upon it by civilized customs and our increased span of life—unless we compensate it for its lost stimuli. Even under savage conditions, as age advances the gums recede and become infected, and the teeth are lost, but for a number of years an almost ideal state of structural and physiological perfection persists like that in fig. 1.

It is interesting also to observe the interdental area of the young rat's tooth. Here again the tissues are firmly adherent to the enamel and there is no interdental space. Indeed, in fig. 3, the rat's molars, one of which is perhaps still only partially erupted, are actually stuck together by the cuticle which is common to both at the contact point, precluding for the moment both caries and pyorrhœa.

In material from civilized man there is, however, always some indication of the constant trauma to which the gum margin, softened by relative disuse, is submitted. There is always a definite periodontal sulcus and, apparently, always some chronic inflammatory infiltration round it (Fish [1]). If the pocket is shallow and its wall firm, abrasion, often amounting to an actual ulceration, is produced at the very edge of the gum at the spot on which the masticatory stress falls when the food slides over the crown of the tooth. Later, when the pocket is deeper, ulcers may be seen at the bottom of the pocket, caused by the continual tearing-back of the pendulous interdental papillæ as the teeth sink into solid food.

As time goes on, the surface of the dead cementum inside the pocket becomes covered with tartar and bathed in serous exudate in which organisms live and multiply; so that apart altogether from a continuance of the trauma which originally caused the lesion, there is a continuous toxic irritation of the ulcerated surface inside the pocket, which prevents healing. The organisms are, however, precluded from actually growing into the tissues by the leucocytes which form the floor of the ulcer in the pocket [2]. Some of these leucocytes are killed from time to time and form pus, which leaks out in a constant ooze.

In just the same way, pus oozes out from a sinus which leads down to a sequestrum of infected necrotic bone. Such a sequestrum also lies in a bed of exactly similar granulation tissue. The processes are strictly comparable and have many essential points in common. In each case there is a necrotic refractory mass of which the tissues cannot rid themselves and which yet harbours germs. In the one case it is necrotic cementum and tartar, in the other necrotic bone. In either case the mass forms a refuge for germs, enabling them to live in full enjoyment of the food and oxygen carried by exuded lymph, yet for the most part out of reach of the leucocytes. The polymorphonuclear leucocytes do indeed venture to the very brink of the lesion



FIG. 1A.—Photomicrograph ($\times 100$) of molar tooth of rat showing early split of keratinous invagination (K), forming a sulcus. N, Nasmyth's membrane. C, Horny cuticle of the gum.

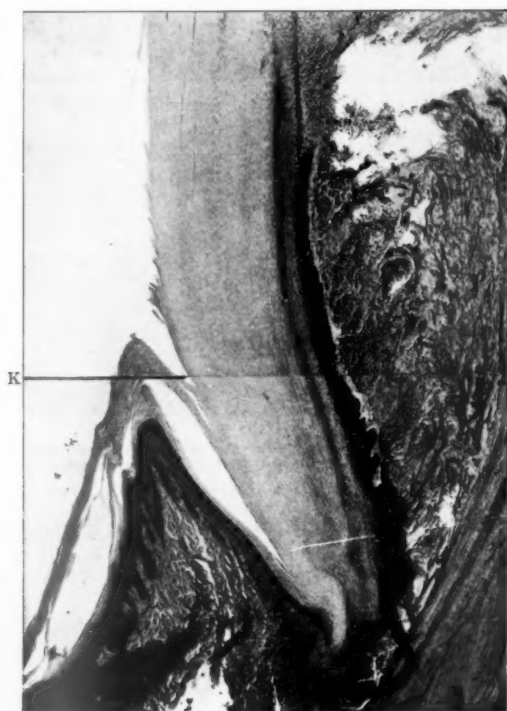


FIG. 2.—Photomicrograph ($\times 46$) of base of finger nail of monkey (Mr. H. B. Harding's specimen), showing a keratinous invagination (K), similar to that in fig. 1, which also displays a tendency to split.

in search of food and, packing solidly, form the floor of the pyorrhœtic ulcer, just as they form the surface of the granulation tissue bed in which the sequestrum lies. Here they wait to catch and devour any stray organism which drifts their way, but if they venture into the pus they will probably never return.

The position is actually one of stalemate and may be demonstrated quite easily without relying on the histological interpretation of the tissue reactions as observed in sections under the microscope. If the organisms do actually penetrate and live in the tissues amongst the cells in the bone and periodontal membrane, then the apex of a pyorrhœtic tooth will always be infected on extraction, whatever we do to the

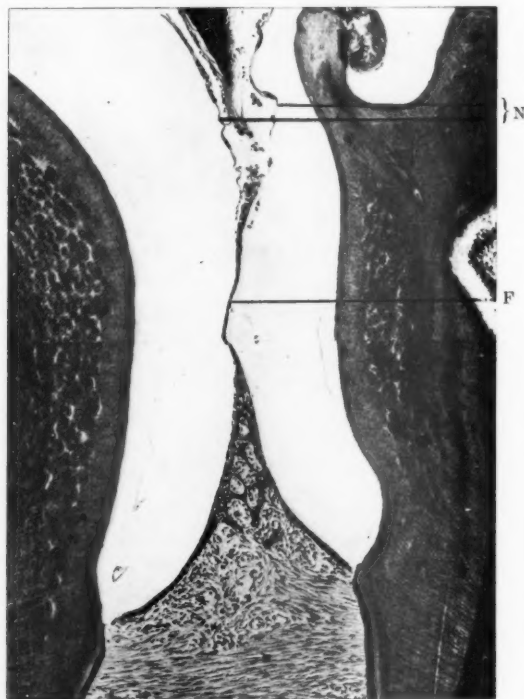


FIG. 3.—Photomicrograph ($\times 100$) of inter dental papilla of rat's molars, showing the Nasmyth's membranes (N) fused at F and healthy tissue filling the whole inter dental space.

pocket. Alternatively, if thorough sterilization of the pocket before extraction enables one to deliver the tooth with a perfectly sterile apex, quite regularly, however severe the pyorrhœa, then it is clear that the infection was entirely confined to the pocket and was killed by the sterilization.

It has been found possible to do this as described in an earlier paper [2] and Dr. Maclean and I have now a series of 30 investigations of teeth extracted from pyorrhœa cases after cauterization of the pocket, all having sterile roots and apices, but such an unblemished record was only obtained by rigorously rejecting any tooth where the cautery wire could not be carried with certainty to the very bottom of the

pocket all round ; or if there was any bleeding which could carry infection from the surrounding teeth or mucous membrane on to the root as it came out, and of course, if the root accidentally hit the lips or other teeth as it came away, it was rejected. We have not yet had a single positive culture where we were satisfied that all these stringent conditions were fulfilled and had predicted a sterile apex.

It seems necessary therefore to accept the histological interpretation, thus supported, that the organisms are confined by a wall of leucocytes to the necrotic surface cells of the ulcers and to similar debris in the pockets. It must then follow that the reaction of the tissues behind the barrier of leucocytes is due to the toxic products of these organisms diffusing into them.

The same reaction is observed in the neighbouring bone whether the irritant be an infected sequestrum of bone or an infected sequestrum of cementum, and also whether the infected cementum be at the neck of a pyorrhœtic tooth or at the apex of a dead one. In each case, toxic products diffuse into the surrounding tissues although the



FIG. 4.—Skiagram of bone necrosis in human lower jaw (by Dr. Blackman from case referred to Mr. Ainsworth). *s* is socket of extracted tooth, forming sequestrum and surrounded by extensive absorption.

organisms themselves cannot penetrate. The result is generally a breakdown of the adjacent connective tissue, whether it be the fibres of the periodontal membrane or the matrix of the bone, though more rarely fibrosis and sclerosis occur. Perhaps the best way of appreciating the effect of this toxic absorption on the bone and the soft connective tissue round pyorrhœtic teeth is to take first a more massive type of reaction where, as the result of trauma, bone is actually invaded by organisms, an acute reaction follows, and a sequestrum is formed ; we may then consider the sequence of events.

Fig. 4 shows the sequestrum infected with organisms forming the centre of an area of widespread bone absorption, yet the sequestrum itself is quite unabsorbed. It consists of the lamina dura or shell of bone which once surrounded the extracted tooth. When the tooth was extracted, organisms were propelled into the vessels in this bone from the periodontal sulcus, as they were into the vessels of the pulp [2],

or of the arm [7]. At that most unfortunate moment, the trauma of extraction bruised the bone forming the socket wall and occluded the vessels imprisoning the germs. These latter made the best of their unique good fortune and, no longer in danger of attack from leucocytes, as they would have been if they had escaped into the general blood-stream, they increased enormously, ate every shred of soft tissue and converted the damaged bone into a bare, infected, necrotic sequestrum—the "dry socket". From this focus the poisons and the germs started to spread in all



FIG. 4A.

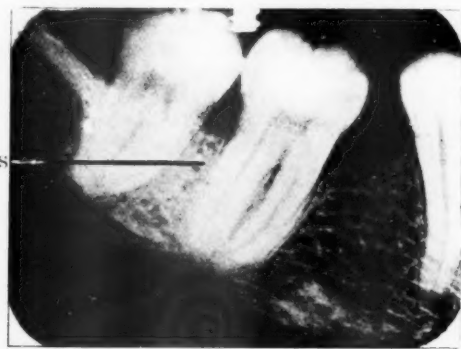


FIG. 4B.



FIG. 4C.

FIGS. 4A, B and C.—Skiagrams of human teeth (by Dr. Blackman) from cases of parodontal infection, illustrating: Bone absorption, A in fig. 4A; bone sclerosis, S, in fig. 4B; Bone absorption, A, and sclerosis, S, in fig. 4C.

directions, although the poisons spread by diffusion more quickly than the non-motile germs could spread by sheer multiplication. In response to this toxic diffusion, leucocytes hurried to the spot. The polymorphonuclear leucocytes got there first and formed their solid barrier as effectively as possible in a tissue which, by virtue of its lacunæ and canaliculi, offers such strategic advantage to the invaders. The leucocytes, nevertheless, at least delayed the spread of the actual organisms, though the poisons continued to diffuse out and irritate the cells of the surrounding bone

behind the wall of leucocytes. The result of this toxic irritation is the absorption of bone which is so very well marked in the skiagram.

Similarly fig. 4A shows an infected sequestrum of cementum and tartar harbouring germs which are prevented from entering the surrounding tissues by the remnant of epithelium and the wall of leucocytes which form the lining of the pyorrhœtic pocket [1]. At the same time the toxic products of this struggle diffuse into the surrounding bone, and again the result is bone absorption.

There are two ways in which the textbooks say that bone can be absorbed; one is by the action of osteoclasts, and the other by halisteresis or vascular absorption. There appears, however, to be no evidence of the existence of the latter phenomenon, and indeed it is by no means clear how it would work. If we accept the rule that inflammatory hyperæmia produces bone absorption, and ischæmia promotes bone deposition (Leriche and Policard [5]), are we willing to overlook or deny that the most active hyperæmia accompanies the opposite phenomenon, to wit repair, when bones are fractured?

Even if we accept the view that, despite the perfect buffering of the blood and tissue fluid, a local inflammatory change in the pH sufficient to use up the alkali reserve and attack the bone salts could take place despite the hyperæmia which is flushing out the tissues, we must still explain how the organic part of the absorbed bone matrix is disposed of. This collagenous material must be digested by a proteolytic ferment which, in turn, can only be produced by a cell, whether we call it an osteoclast or anything else.

The theory of bone absorption by halisteresis may perhaps have been devised because it is not often that we see osteoclasts actually at work, and realizing this difficulty, Hopewell-Smith [4] suggested that even the round cells are capable of absorbing the bone; yet in fact we would not expect to see osteoclasts at work very often. It may not be generally recognized that they work very quickly and then break up and disappear. Gottlieb and Orban [3], however, showed that if a tooth is moved, in a dog, by means of an appliance, a considerable part of the interdental septum is absorbed away by newly formed osteoclasts in as little as thirty-six hours. At this rate the osteoclasts could eat the whole skeleton in a few months, as indeed they very nearly do in cases of parathyroid tumour.

In a chronic disease like pyorrhœa, therefore, we find a very large number of Howship's lacunæ in which osteoclasts, having previously removed a contaminated fragment of bone matrix, have now disintegrated and disappeared, so that only a very occasional one is actually caught in the act (figs. 5 and 5A).

If the irritation becomes too severe, the osteoclasts break up and are replaced by round cells, as was shown by Stewart-Ross [9] when he infected the dentine experimentally from the root canal. At first the permeable apical cementum was absorbed in his experiments, then as the tubules of the dentine were opened up, the released toxic material killed the osteoclasts, whereupon leucocytes entered and filled the lacunæ. This often happens if an acute infection spreads towards an osteoclast; as the toxicity of its environment increases, the osteoclast is killed and replaced by cellular infiltration (fig. 5, R). In this way, Hopewell-Smith's observation is explained. Conversely, if the irritant is diminished, the cellular infiltration and the osteoclasts disappear and osteoblasts are stimulated by the fading irritant to build up the bone again and fill in the lacunæ, as is shown hundreds of times throughout the bone in fig. 5, or in any long-standing case of pyorrhœa.

Observations on chronic inflammatory reactions in connective tissue suggest, therefore, the following summary:—

During the invasion, streptococci having a tendency to grow into the tissues are met by a wall of polymorphonuclear leucocytes, while their toxic products diffusing into the surrounding tissues are encountered by round-celled infiltration. When repair sets in, wandering cells (histiocytes or macrophages) eat up the soft

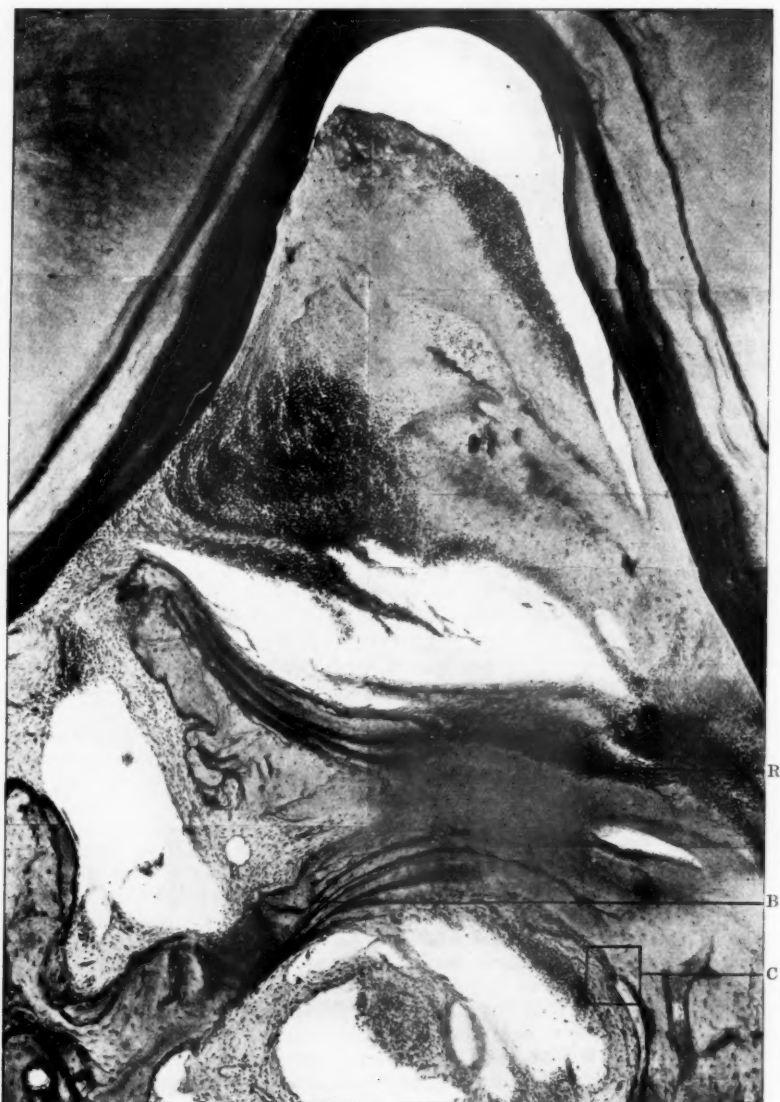


FIG. 5.—Photomicrograph ($\times 60$) of parodontal pocket (human) extending between the roots of a lower molar, showing numerous Howship's lacunæ from which the osteoclasts have disappeared and been replaced by round cells (R) where the toxic irritation has increased. At B, where the irritation has subsided, the Howship's lacunæ are built up again with bone matrix and at C (see fig. 5A) an active osteoclast is to be seen.

tissue debris, while fibroblasts are stimulated to produce scar tissue or "fibrosis" as the irritant is diluted and removed.

Similarly osteoclasts, formed in response to toxic irritation, eat the contaminated bone, while if the irritant becomes diluted, or if it is less severe, osteoblasts are stimulated to lay down new bone and produce "sclerosis." Osteoclasts never phagocytose either living or dead organisms, and are killed by too severe a poison or by the actual presence of streptococci.

The sequence of events, therefore, in such a case of suppurative osteitis as that illustrated in fig. 4, becomes clear.

The organisms being trapped in the damaged bone of the socket, the surrounding bone matrix becomes contaminated by their soluble toxic products which diffuse along the lymphatics and into the canaliculi of the matrix. This stimulates the production of osteoclasts at an appropriate distance from the infection, and unless these osteoclasts can clear away a zone of bone around the infected area before the organisms can reach them, they will be killed and the necrosis will continue to spread

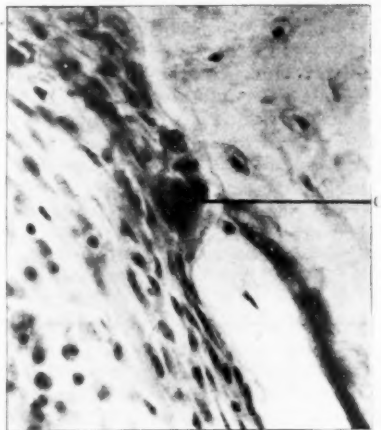


FIG. 5A.—Higher magnification of fig. 5 ($\times 412$). c is one of the few osteoclasts to be found.

If, however, the osteoclasts accomplish their task in time, the sequestrum becomes separated from the rest of the bone and the gap is filled by a safety barrier of leucocytes. The organisms spread to the edge of the sequestrum but cannot cross the gap because of the leucocytes. Absorption of the surrounding bone on the other side of the gap, however, continues as long as the poisons diffuse into it, that is, until the sequestrum with its colony of organisms is taken away. The dead infected bone can never be absorbed, unless at a much later date the infection dies out of it and it becomes a sterile foreign body.

The Howship's lacunæ seen on the surface of all sequestra were cut by osteoclasts before the actual infection reached the periphery. Similarly, the living bone of the alveolar crest near a pyorrhœa pocket, being uninfected, is absorbed, yet the cementum in the pocket, being infected, is not absorbed. The apex of a dead tooth may be absorbed while toxic material only is escaping from the infected root-canals into the bone, but if the infection itself reaches the osteoclasts they die, pus fills the lacunæ, and absorption ceases. A peri-apical rarefaction area is evidence of past toxic irritation, not necessarily of present infection; though the once irritated area may have

become infected or may be still the site of toxic irritation. If all irritation had entirely gone, new bone would have appeared and filled the gap.

In fig. 4A the alveolar crest, and even the deeper bone, is absorbed because the toxic matter diffusing into it was sufficiently irritating to stimulate the embryonic mesoderm cells to produce osteoclasts, which have now disappeared and been replaced by round cells. In fig. 4B, which is taken from a patient with a clinically clean mouth, the toxic diffusion is much smaller in amount and not so highly irritating, hence only osteoblasts were stimulated and sclerosis of bone was produced round the pocket. In fig. 4C, both grades of irritation are seen. Absorption of the crest of the alveolar bone and sclerosis at a lower level where the toxic matter had become diluted in the tissues.

In each case the toxic diffusion follows the path of lymphatic drainage from the gum margin, as described by Macgregor [6]; and before leaving the local sequelæ of infection in the sulcus the possibility of actual organisms being thrust into the lymphatic vessels of the gum margin and periodontal membrane must be considered. No harm would be likely to follow if the organisms were carried direct to the lymph-nodes, but not infrequently they become arrested halfway down the periodontal membrane—perhaps by the pressure of the lingual bar of a denture or at other times just owing to temporary stasis in the lymphatic channel. This commonly occurs between the upper lateral and canine, and the result is, as occurs elsewhere in the body under similar circumstances, acute suppurative lymphangitis.

The condition is recognized clinically as a parodontal abscess. The tooth concerned becomes very tender to pressure, a continuous gnawing pain is experienced, the gum margin is red and swollen, and ultimately the pus points either through the alveolus or into the pocket, thereby enormously deepening it overnight. The condition is significant as showing how impossible is the conception that these mouth organisms really have their normal habitat in the tissues.

REMOTE SEQUELÆ OF PARODONTAL INFECTION

In view of this evidence it is possible to assess very accurately the dangers of pyorrhœa to the patient's general health, and to place the true value upon any method of treatment which may be devised. The danger to health is first from the bacterial shower into the blood-stream which occurs on eating [8], or on extraction of the teeth [7]. Normally this transient bacteræmia disappears very rapidly and does no harm, but there are exceptions. The organism may, as Okell and Elliott suggest, become implanted on a fibrinous vegetation of a heart valve in cases of active endocarditis, since these fragments of non-vital fibrin lie actually in the blood-stream and offer a safe breeding ground for the germs. The result is a fatal bacterial endocarditis which in 95% of cases is due to *Streptococcus viridans*, the true mouth streptococcus; but much may be done to avoid such a catastrophe.

If possible no tooth should be extracted while fibrinous vegetations are still present. Any living tooth necessarily extracted on account of pain should have the periodontal sulcus cauterized first; it is then quite safe to extract it, but it would be wiser to treat the pulpitis with arsenic. The extraction of any dead tooth is, however, still a grave danger even if the pocket has been cauterized. It should only be extracted if an acute abscess forms and causes severe pain, and of course the sulcus must still be cauterized. Even so, we have found that with a dead tooth a bacteræmia may occur from the infected apex alone, even after the sulcus has been cauterized, so this risk should not be lightly taken.

If, however, a patient with active non-infective endocarditis has severe pyorrhœa with heavy granulations round the gum margins, he is in very serious danger even if we do not interfere surgically. The risk of a bacteræmia from chewing is so grave that he should be put on a soft diet. He must not brush or rub the gums while the

heart vegetations are present, but may only hold very hot mouth washes, such as permanganate of potash and peroxide of hydrogen, in his mouth frequently.

The vegetations may persist, however, for a long time, and the danger of a shower from eating is so grave that it is a matter of great urgency to devise a method of treating these cases. It is not safe to leave the mouth condition as it is, much less, of course, to extract the teeth or even manipulate the gums. We have even had a positive blood culture after simple scaling. It is really a choice of evils; gingivectomy will cure the pyorrhœa, but may cause a bacterial shower. In one case out of four Dr. Maclean and I have found this to occur, though it may depend on the dexterity with which the operation is performed. Perhaps the safest course is to pack the pockets with zinc oxide and oil of cloves, mixed rather thin and incorporated with wisps of cotton-wool. This dressing is tucked, rather than packed, into the pockets with the utmost gentleness. Mr. Arthur Bulleid tells me he has observed histologically that, if properly carried out, this treatment eliminates all pus from the pockets for the time being. This agrees with clinical experience and it would therefore appear to be our best safeguard in all such cases. The dressing can, of course be repeated every few days throughout the acute phase of the illness, and as the inflammation subsides, scaling, and even gingivectomy, may be carried out quite safely.

A second danger from a bacterial shower, which may occur in anyone however healthy otherwise, is that during the few minutes, or possibly hours, that the organisms are circulating in the blood, the individual may bruise a bone and imprison some of the bacteria in the clot. If this happens there is nothing whatever to prevent them growing and setting up an osteomyelitis in, for example, the tibia, in just the same way as necrosis was produced in the mandible by damaging the alveolus during extraction at a moment when the vessels in that bone were carrying the infection which had just been thrust into them by the pumping action of the forceps.

On the other hand, the bruising of a bone at a time when the blood is sterile, is not liable to produce infective osteomyelitis, since a subsequent bacteræmia cannot introduce organisms into a vessel which is already thrombosed in the bruised bone. Nor, even, will mouth organisms penetrate into the bone of a socket after tooth extraction if they were not trapped in it at the time. The streptococci and staphylococci are not motile, whereas leucocytes are; and the injured vessels do not remain open for germs to be swept in but are closed by blood-clot at once. Even burnishing infected saliva into newly opened bone, as is often done with an elevator in the socket of a partially extracted tooth, generally fails to infect the bone.

Apparently the only other possible danger from a bacterial shower, since septicæmia from it is uncommon, is that these organisms, temporarily in the blood-stream, might find a home in such places as the joints and ends of the bones, thereby producing arthritis, or perhaps in fibrous tissue, producing fibrositis. We have, however, shown [2], that the streptococci can only continue to exist in the tissues if they establish a necrotic nidus, which in this case would have to be a pyæmic abscess. No such lesions have ever been demonstrated in the tissues in fibrositis or rheumatoid arthritis although they would be very easy to demonstrate if they were there. It may, therefore, be assumed that the effect of oral sepsis on these diseases is due to the absorption of soluble toxic material and not to the direct spread of the germs themselves to the site of the lesion.

To summarize, therefore, the theoretical position is that the bacteræmia of pyorrhœa is only of danger to a patient suffering from active, non-infective endocarditis, or, in the case of a healthy patient, if trauma to a bone should occur at a moment when the organisms are present in the vessels at the site of such injury. Three clinical cases of the former catastrophe have come within the author's experience recently, while the clinical incidence of "dry" socket is strong evidence of the latter view since it occurs only when the bone is badly bruised at the moment of extraction, that is, at the moment of invasion by organisms. It has, in recent months, been entirely

eliminated from the author's practice by cauterizing the gum margin in doubtful cases before extraction.

The chronic toxic absorption into the tissues is, however, a more constant menace though perhaps not so dramatic. Not only do the soluble toxic products of the organisms' activity in the sulcus diffuse into the periodontal membrane and alveolar bone and therefore destroy the attachment of the teeth but, being taken into the general circulation, they are liable to irritate other remote tissues, as shown by Dr. Graham.¹ The defence against this poison is twofold. The round cells, chiefly lymphocytes, which infiltrate the parodontal tissues are a response to the presence of the poison locally, and presumably destroy it to some extent, otherwise they would hardly be likely to be so constantly attracted by it. Secondly, much of the toxic matter is carried away by the lymph-stream [6], as is shown by the chronic lymphangitis which surrounds the lymphatics [1]. This poison will, therefore, meet a further large number of lymphocytes in the lymph-nodes.

There is, however, a mass of clinical evidence that a considerable amount passes into the general circulation, and before it is ultimately destroyed in the liver and kidneys, which form the second line of defence, it may irritate any tissues which are inherently susceptible and temporarily sensitized, such as the joints and fibrous tissue generally. It is significant that these structures are composed of the same type of connective tissue as the parodontal tissues themselves. Moreover the morbid changes in infective arthritis, which include bone absorption and "sclerosis" or lipping, round-celled infiltration, and fibrous tissue breakdown or hypertrophy (Willcox [10]), are very similar to the changes which occur in the parodontal tissues in response to irritation from the toxic material in pyorrhætic pockets.

Fig. 6 shows a skiagram of the hand of a patient suffering from rheumatoid arthritis. The bone absorption round the joints is well marked. In fig. 7, another case of infective arthritis, there is sclerosis or bone deposition, particularly on the iliac side of the joint, though this is a less common phenomenon in the infective type than in simple osteo-arthritis.

When, therefore, a patient exhibits, on the one hand, inflammatory and degenerative changes described as fibrositis or arthritis in the connective tissue generally, and at the same time exhibits an ulcerated gum margin, and is absorbing poisons from it which are causing hypertrophy, or destroying the same sort of tissue in the jaw in exactly the same way, it seems reasonable to associate the two conditions. How far the extent of the local tissue destruction may be taken as a measure of the damage being done to the more remote structures is a matter of conjecture, but it seems unlikely that much harm can be caused by the diluted toxic material to a distant joint if the concentrated poison at the point of entry is not causing sufficient irritation to destroy or affect the local connective tissue. The radiographic demonstration of local bone destruction or sclerosis is at least a very useful indication that toxic absorption is taking place, and the absence of any local radiographic change in the bone is not without its significance.

Patients vary very widely in their sensitivity to this toxic matter; one will show widespread bone destruction with only very slight pocketing or ulceration, while another may suffer very little local bone damage from quite extensive and old-standing "dirt pyorrhœa". Such inherent frailty, or resistance, in the patient's protoplasm—or perhaps it is acquired susceptibility or immunity to toxic irritation—may not be present in all the tissues of the body. Structures under constant strain may succumb more readily, and it must be admitted that toxic matter which fails to stimulate the production of osteoclasts at the point of entry may nevertheless irritate such tissues as the retina, or a joint which has been sprained, even when in much greater dilution. It does not seem reasonable, however, to extract a dead tooth with no radiographic or clinical sign of bone change round it if the patient is in good health, since in such a case there are for the moment neither local nor general signs of toxic absorption.

¹ *Proc. Roy. Soc. Med.*, 1937, **30**, 1155 (Sect. OJont., 51).



FIG. 6.—Skiagram (by Dr. Rohan Williams) of infective arthritis of hand (human) showing bone absorption.



FIG. 7.—Skiagram (by Dr. Rohan Williams) of infective arthritis of sacro-iliac joint (human), showing sclerosis especially on the iliac side of the joint.

On the other hand, certain obvious indications for thorough eradication of all doubtful or even possible sources of toxic absorption do constantly occur. Derangement of the liver or kidney function is perhaps the most certain, since these organs are ultimately responsible for the elimination of the poisons. Similarly, in pharyngitis and gastro-intestinal disease, the danger of swallowing irritating discharges must not be overlooked. Even in respiratory disease, such as asthma, two recent cases of a dramatic recovery following gingivectomy illustrate an association of these conditions with oral sepsis which has been recognized in some quarters for a very long time.

ELIMINATION OF PARODONTAL INFECTION

The list might be considerably extended, but only by encroaching on the province of the general physician. It is, however, very important that we, as physicians of the mouth, when called upon to eliminate the possibility of toxic absorption or a bacterial shower from the parodontal tissues, should do so thoroughly and completely and not merely carry out an isolated dramatic operation. It is not of much benefit to the patient to extract a useful, but dead, front tooth because there is a trace of periapical bone absorption present and yet to leave the gum margins round the back teeth ulcerated, inflamed, and liable to bleed at a touch. Incidentally such an operation is also seriously misleading to the general physician. There is more toxic absorption, as shown by the soft tissue ulceration and bone loss round these periodontal sulci, than could possibly have been taking place from the infected apex, and the organisms are the same in each case. The patient would be much healthier and happier if the chronic inflammation round the back teeth had been cured and the front tooth left; though, of course, both areas should be treated. Perhaps apicectomy of the front tooth would have been effective.

Similarly, it is almost impossible to find a case in which a few teeth are so badly affected by pyorrhœa that they have to be extracted and yet the rest of the teeth are not in need of any treatment at all. It is almost invariably necessary to carry out a toilet of the gum margins round the remaining teeth if the patient is not to lose all possible advantage from the extractions. It may be that our failure to complete the eradication of sepsis in such cases has often misled physicians, and made them, as well as the general public, wonder whether oral infection is indeed a factor at all in general disease. Certainly we cannot expect any clear-cut results from such mismanaged experiments.

Even if all the teeth are extracted, the operation may be associated with so much physical and mental trauma and such a flood of toxic matter and actual bacteria into the blood-stream that the patient is often irreparably damaged, whatever he may ultimately gain.

It is, however, seldom necessary to extract all the teeth. Even teeth which are slightly loose are far more useful than most dentures. Once it is realized that, if a tooth is reasonably firm and its pockets can be cut away without leaving it absurdly denuded, it is thereby made quite healthy, a very large number of teeth may be saved which are at present extracted, and the deformity and discomfort of full dentures will be avoided. Even if the patient's general health does not improve, he has gained by the treatment and is the better for having a clean mouth and most of his teeth intact. He has not lost all his teeth and gained nothing; moreover, he will be grateful, not disgruntled.

Wholesale extractions may lead to very serious disability, and it is no wonder that a physician hesitates to expose a patient to the risk of edentulous misery which may well be worse than the original disease; but he nevertheless wishes his patient to have a clean mouth if it can remain intact; and no patient, if he realized it, would willingly have a chain of suppurating sores in his mouth—more loathsome than a festering boil on the surface of his body.

To turn for a moment to the actual treatment of parodontal infection. The demonstration that the organisms are all lodged superficially in the pocket has allayed any misgiving about the necessity of treating, or maltreating, the underlying bone which was previously thought to be infected. It is only necessary to cut away the pockets to ensure that the organisms shall lose the crevice in which they found sanctuary. The pernicious association of the infected sequestrum of cementum and the granulation tissue bed of the ulcer is broken up. Moreover, if we can render the epithelial covering of the gums accessible to the patient's efforts at mouth hygiene, the horny cuticle of the gum can be restored by friction right up to its attachment to the tooth. The toxic absorption will cease completely, for the poison cannot penetrate the horny cuticle, and we can give an assurance that the teeth are as void of offence as any teeth can be.

If, however, the disease is too far advanced, or through lack of co-operation, the patient or the dental surgeon fails to secure firm keratinization right up to the cement attachment, so that granulations remain, the only cure is to extract the tooth concerned. Mr. Arthur Bulleid has pointed out that a perfect control of the success, or otherwise, of the treatment is the continued presence or absence of pus cells at the neck of the tooth. With this dictum the author emphatically agrees, but would crave indulgence, for it is difficult to obtain complete success in any human endeavour, and a few pus cells can generally be found at the gum margins between the back teeth of even people with very clean mouths; so much so that somebody once described the leucocyte as a normal inhabitant of the sulcus. Such a view was, of course, misguided, but to show that we have cured pyorrhœa, we must undoubtedly eliminate the possibility of there being any marked collection of pus cells at the gum margins.

Fortunately it is seldom necessary even now to extract the tooth in order to do this, and we may surely hope that, by constant effort to save every living tooth and render it healthy, our methods will become simplified and improved and the reproach of wholesale extraction be lifted from us.

The author wishes to express his indebtedness to Sir William Willcox for his advice and to Dr. Maclean for his continued co-operation; to Mr. Ainsworth, Dr. Blackman, and Dr. Rohan Williams for the loan of skiagrams; to Mr. Harding for the loan of a section, and to the Medical Research Council for a grant towards the cost of the experimental work involved.

REFERENCES

- 1 FISH, E. W., *Brit. Dent. J.*, 1935, **58**, 531.
- 2 FISH, E. W., and MACLEAN, I. H., *Brit. Dent. J.*, 1936, **61**, 336.
- 3 GOTTLIEB, B., and ORBAN, B., "Die Veränderungen der Gewebe bei übermässiger Beanspruchung der Zähne", Leipzig, p. 26.
- 4 HOPEWELL-SMITH, A., "The Normal and Pathological Histology of the Mouth", 1919.
- 5 LERICHE, R., and POLICARD, A., "The Normal and Pathological Physiology of Bone", (Trans.), London, 1928.
- 6 MACGREGOR, A., *Proc. Roy. Soc. Med.*, 1936, **29**, 1237.
- 7 OKELL, C. C., and ELLIOTT, S. D., *Lancet*, 1935 (ii), 869.
- 8 ROUND, H., KIRKPATRICK, H. J. R., and HALL, C. G., *Proc. Roy. Soc. Med.*, 1935, **29**, 1572.
- 9 STEWART-ROSS, W., *Brit. Dent. J.*, 1935, **58**, 473.
- 10 WILLCOX, W. H., *Brit. M. J.*, 1921 (i), 804.

The Toxicity of Sterile Filtrate from Parodontal Pockets

By J. WALLACE GRAHAM, M.D., D.D.S., M.R.C.P.

ABSTRACT.—The local effect of the absorption of toxic material from pyorrhœa pockets on the hard and soft tissues around the teeth is well known. In this experiment an attempt was made to study the toxic effect on remote structures by injecting the sterile filtrate fresh from pyorrhœa pockets into various animals.

The filtrate was obtained from patients with chronic pyorrhœa by removing the contents from parodontal pockets and passing them through a Seitz filter. The sterile filtrate obtained was then injected into cats, guinea-pigs, rabbits, and rats, in varying amounts.

In the group of four cats, all showed fatty degeneration of the liver and two showed extreme fatty degeneration of the kidney tubules.

Five guinea-pigs receiving one injection of $\frac{1}{2}$ c.c. of filtrate showed no pathological change in the liver or kidney. One out of three guinea-pigs receiving two injections of filtrate showed fatty degeneration of the liver, while five out of six pigs receiving one injection of 1 c.c.,—i.e. double the quantity—showed definite fatty degeneration of the liver. One out of two rabbits showed similar changes and of six rats injected, all died in from five to seven days.

The experiment suggests that substances are elaborated in paradental pockets which are highly toxic and tend to injure the liver and kidney of animals in the process of their elimination. Such toxic material proved fatal in fifteen of the twenty-five animals injected.

RÉSUMÉ.—L'effet local de l'absorption de matières toxiques des poches pyorrhéales sur les tissus durs et mous entourant les dents sont bien connus. Dans cette expérience l'auteur a cherché à étudier l'effet toxique sur les tissus éloignés par l'injection chez divers animaux d'un filtrat stérile frais du contenu de la poche pyorrhéale.

Le filtrat fut obtenu chez des cas de pyorrhée chronique, par la collection du contenu des poches paradentaires, et son passage par un filtre de Seitz. Le filtrat stérile fut injecté en doses diverses dans des chats, des cobayes, des lapins et des rats.

Sur quatre chat injectés, quatre montrèrent une dégénération graisseuse du foie, et deux une dégénération graisseuse extrême des tubules rénaux.

Cinq cobayes recevant une seule injection de $\frac{1}{2}$ c.c. de filtrat ne montrèrent aucun changement pathologique du foie ou des reins. Sur trois cobayes recevant deux injections, un montra une dégénération graisseuse du foie, et cinq cobayes sur six recevant une injection de 1 c.c., c'est-à-dire deux fois autant, montrèrent une dégénération graisseuse distincte du foie. Un lapin sur deux montra des changements analogues, et six rats injectés moururent après 5 à 7 jours.

Cette expérience indique que des matières très toxiques se produisent dans les poches paradentaires, tendant à endommager le foie et les reins des animaux aux cours de leur élimination. Cette matière toxique a exercé un effet létal sur 15 des 25 animaux injectés.

ZUSAMMENFASSUNG.—Die örtliche Wirkung der Resorption von toxischem Material aus pyorrhöischen Taschen auf die die Zähne umgebenden harten und weichen Gewebe ist gut bekannt. Die vorliegenden an verschiedenen Tieren angestellten Experimente stellen einen Versuch dar, die Fernwirkung der Injektion von frischen sterilen Filtraten aus pyorrhöischen Taschen zu untersuchen.

Das Filtrat wurde von Patienten mit chronischer Pyorrhoe in der Weise gewonnen, dass der Inhalt paradentaler Taschen durch ein Seitz Filter filtriert wurde. Verschiedene Mengen des so erhaltenen sterilen Filtrates wurden dann Katzen, Meerschweinchen, Kaninchen und Ratten injiziert.

Vier Katzen zeigten alle fettige Entartung der Leber und zwei zeigten höchstgradige fettige Entartung der Nierentubuli.

Fünf Meerschweinchen zeigten nach der Injektion von $\frac{1}{2}$ ccm. Filtrat weder in der Leber noch in den Nieren irgendwelche pathologischen Veränderungen. Nach 2 Injektionen von Filtrat zeigte 1 von 3 Meerschweinchen fettige Entartung der Leber, während von 6 Meerschweinchen, die eine Injektion von 1 ccm., das heisst zweimal so viel, erhielten, fünf deutliche fettige Entartung der Leber aufwiesen. Eines von zwei Kaninchen zeigte ähnliche Veränderungen; von 6 Ratten starben alle 5-7 Tage nach der Injektion.

Die Versuche legen die Annahme nahe, dass sich in den paradentalen Taschen hochgiftige Stoffe bilden, die bei ihrer Ausscheidung zu einer Leber- und Nierenschädigung der Tiere führen können. Die Injektion derartiger toxischer Stoffe erwies sich bei 15 von 25 Versuchstieren als tödlich.

THE experimental work to be presented arose from the paper given by Dr. E. W. Fish and Dr. I. Maclean at the Empire Dental Meeting last July. In this paper the authors suggested that the round-celled infiltration of the gum margin seen in pyorrhoea was the cellular response to toxic material diffusing into the tissues from the infected pocket, and was not due to the actual presence of organisms amongst the tissue cells. Such toxic material was said to initiate osteoclastic action which, over a period of time, led to the destruction of the alveolar bony crests and the other

local effects of pyorrhœa with which we are all familiar. The authors also suggested that, should the source of irritation be less severe, osteoblasts, rather than osteoclasts, might be stimulated, giving rise to new bone formation and the condition radiographically described as sclerosis.

The elaboration of an exotoxin by the organisms present in a parodontal pocket has never been demonstrated or claimed. It was not likely therefore that the toxic material responsible for the above changes about the teeth could be obtained from cultures of the organisms present, but it was possible that decomposition products formed in the pocket might be toxic, and that the actual material from the pocket might give different results. Accordingly, it was decided to take the contents fresh from pyorrhœa pockets, and to test the effect of their immediate injection into animals. The nature of the substance injected was unknown, but the effect of introducing various other poisons into the body has been carefully worked out, and it was reasonable to expect that certain pathological changes would occur.

The effect of an exotoxin, for instance, is well seen in diphtheria, in which the lesion may remain localized in the nose, throat or larynx, and at no time does the organism invade the blood-stream, but the products of bacterial activity give rise to the extreme toxæmia which is characteristic of the disease and which may bring it to a fatal conclusion. Similarly the effect of the administration of various mineral and organic poisons has been studied and has been seen to fall particularly on the liver, as was pointed out by Sir William Willcox in the Lumleian Lectures of 1931.

When a poison is introduced into the body certain protective mechanisms are brought into play, and in this respect the liver has a most important function in protecting the body against exogenous toxic substances. Willcox refers to this action as the "toxiphylactic function of the liver". If the poison is absorbed from the alimentary tract it is conveyed by the portal blood-stream to the liver, which acts as the first line of defence. When the poisons are introduced into the general circulation—as for example the arsenobenzol derivatives—the liver absorbs much of the poison from the blood-stream and so protects the other tissues of the body. In exerting this prophylactic function the liver itself often suffers severely and its cells may undergo cloudy swelling, fatty degeneration, or even extensive necrosis, depending upon the nature of the poison absorbed. In addition, an inflammation of the interstitial tissues may be set up and a progressive hepatitis with fibrosis result. The kidney, also, serves a useful function in eliminating exogenous toxic substances.

The local effects of the toxic material in parodontal pockets is clearly defined and has been dealt with in the previous paper. The question arises: Does this material go further and, like some of the poisons mentioned above, cause pathological changes in the viscera?

Method.—The toxic material was collected from patients attending the Parodontal Clinic of the Royal Dental Hospital. Only patients with chronic pyorrhœa were used and no material from acute cases—such as those of ulcerative gingivitis—was used in this experiment.

About 2 c.c. of sterile Ringer's solution was placed in a beaker, and the material in the pockets was removed with ordinary scalers and transferred to the Ringer's solution. After approximately twenty minutes' scaling, the result was a fairly concentrated solution of bacteria, calculus, cellular, and food detritus, and a few blood-cells. The septic solution was then passed through a Seitz filter to remove all bacteria, as we wished to test only the toxic material already formed in the pocket. Filtration was carried out with the aid of a Geissler pump, and a loop of the filtrate was then taken for culture to check its sterility. Usually about $\frac{1}{2}$ to 1 c.c. of filtrate was obtained for injection into various animals.

The result of these injections was at first rather speculative; therefore various amounts and ways of injection were used. In an effort to produce local as well as general effects, the injections were made into the gingival tissues of cats in the upper

premolar region, a control injection of Ringer's solution being made on the opposite side. An anaesthetic was necessary and a mixture of chloroform and ether was at first used. Later when liver changes were found at autopsy, ether alone was used. No anaesthetic was necessary for guinea-pigs, rabbits, or rats. Control animals, living under the same conditions, were killed from time to time, corresponding to the death of the injected animals.

Results.—The first group of animals consisted of four cats (Table I). One died four days after an injection of $\frac{1}{2}$ c.c. of filtrate into the gingival tissues. The second cat died sixteen days after a similar injection. The third and fourth cats received 18 and 16 injections, respectively, of a slightly smaller dose over a period of ten

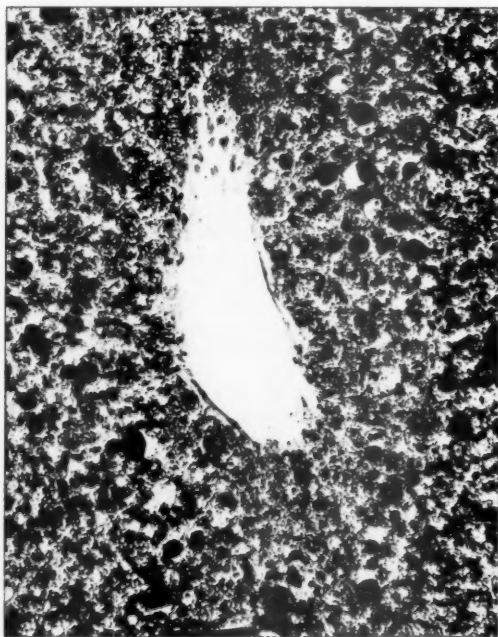


FIG. 1.—Cat No. IV. Section of liver, showing fatty degeneration and infiltration in the central vein area. (Sudan III stain) $\times 187$.

weeks and were then killed. Cat No. III, after two injections, became acutely ill, refused its food and in ten days was markedly emaciated. At this time it gave birth to four stillborn kittens. During the acute illness, the injections were discontinued and then recommenced on recovery. This cat was given an anaesthetic of chloroform and ether. Cat No. IV received 16 injections over a period of ten weeks, but ether alone was used as an anaesthetic.

At autopsy the livers were found to be paler than normal and rather yellowish in colour. They were slightly swollen with rounded edges, and in the case of Cats III and IV were definitely greasy to cut. Sections were made of the liver in Cats I and

II, and of the liver, kidney, and jaws in Cats III and IV. The liver sections stained with Sudan III revealed in all four cats definite fatty degeneration and in some cases infiltration, chiefly in the central areas of the liver. The liver cells in this area were filled with fine droplets of fat, associated with evidence of cellular disintegration: the parenchyma elsewhere being normal (fig. 1).

TABLE I.—CATS.

Animal	No. and amount of injections	Died or killed	Time	Liver	Kidney
I	1 × 0.5 c.c.	Died	4 days	+	—
II	1 × 0.5 c.c.	Died	16 days	++	—
III	18 × 0.3 c.c.	Killed	10 weeks	++	++
IV	16 × 0.3 c.c.	Killed	10 weeks	+++	+++
Control 1	0	Killed	4 days	0	0
Control 2	0	Killed	10 weeks	++	0
Control 3	0	Killed	10 weeks	0	0



FIG. 2.—Cat No. IV. Section of kidney, showing extreme fatty degeneration of the tubules with no change in the glomeruli. (Sudan III stain) × 176.

The kidneys of Cats III and IV appeared normal in the gross specimen but microscopically showed extreme fatty degeneration in the tubules, in striking contrast to the normal kidney, which shows no fat in the tubules. The glomeruli were normal so that the condition could not be due to any form of nephritis (fig. 2). The cat which

received only ether as an anæsthetic showed the most severe changes of any of the series.

No pathological changes were found in sections of the jaws at the point of injection, which was a reasonable expectation as the bony changes in parodontal disease occur only after years of constant absorption of such toxic material.

Three control cats were killed at this time, one of which showed moderate fatty changes in the liver but none in the kidneys. The other two showed no changes in the liver or kidneys.

The second group of animals consisted of 14 guinea-pigs with controls (Table II).

5 were given 1 injection of $\frac{1}{2}$ c.c. of filtrate.

3 were given 2 injections of $\frac{1}{2}$ c.c. of filtrate, with an interval of ten days between.

6 were given 1 injection of 1 c.c. of filtrate.

TABLE II.—GUINEA-PIGS.

Animal	No. and amount of injections	Died or killed	Time days	Liver	Kidney
19/37	1 \times $\frac{1}{2}$ c.c.	Died	4	0	0
25/37	1 \times $\frac{1}{2}$ c.c.	Died	9	0	0
24/37	1 \times $\frac{1}{2}$ c.c.	Died	9	0	0
21/37	1 \times $\frac{1}{2}$ c.c.	Died	10	0	0
43/37	1 \times $\frac{1}{2}$ c.c.	Killed	13	0	0
22/37	2 \times $\frac{1}{2}$ c.c.	Died	20	0	0
39/37	2 \times $\frac{1}{2}$ c.c.	Killed	23	+	0
41/37	2 \times $\frac{1}{2}$ c.c.	Killed	23	0	0
176/36	1 \times 1 c.c.	Died	4	+	0
3/37	1 \times 1 c.c.	Died	4	+	0
27/37	1 \times 1 c.c.	Died	9	0	0
45/37	1 \times 1 c.c.	Killed	13	+	0
47/37	1 \times 1 c.c.	Killed	13	++	0
59/37	1 \times 1 c.c.	Killed	13	++	0

Eight of the 14 pigs died following the injection, in an average of eight days. Although the toxicity of the filtrate was in no way standardized, it is interesting to note that none of the pigs having one injection of $\frac{1}{2}$ c.c. showed pathological changes. One out of three pigs having two injections of $\frac{1}{2}$ c.c. showed definite liver changes, but five out of six pigs having one injection of 1 c.c., i.e. double the previous quantity, showed definite liver changes (fig. 3). Control animals showed no change in either liver or kidney.

Two rabbits only have been injected up to the present time. One rabbit was given 1.5 c.c. of filtrate intravenously into the ear vein. In a few days, like Cat III, it became acutely ill, refused its food and in ten days was severely emaciated. Blood cultures taken during the acute illness were negative. The animal survived the acute phase and was kept alive for ten weeks. Sections of the liver stained with Sudan III showed slight fatty degeneration in the central areas, and hæmatoxylin and eosin stains showed a diffuse cloudy swelling of the parenchyma. The kidneys showed no pathological change. A second rabbit was given 2 c.c. of filtrate subcutaneously and was killed in thirteen days. No pathological changes could be found in this animal.

Five rats were given one injection of $\frac{1}{2}$ c.c. of filtrate. All died in five to seven days but sections of the liver and kidney showed no appreciable change.

Discussion.—The results obtained from this preliminary series of animals cannot be regarded as conclusive evidence of the precise effect of the filtrate from parodontal pockets.

It is well known that fatty degeneration occurs in laboratory animals which are underfed, but in the series of controls used in this experiment only one cat showed fatty degeneration in the liver and no change in the kidney, which is in striking contrast to the cats receiving the injections.

The variation in the time of death and in the pathological findings is to be expected, as it was not possible both to standardize the dosage and also inject it fresh from the pocket.

The experiment does however suggest that substances are elaborated in parodontal pockets which are highly toxic and tend to injure the liver and kidney of

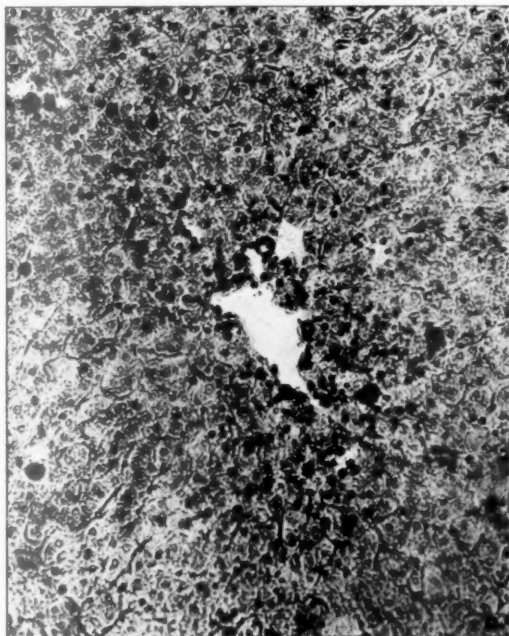


FIG. 3.—Guinea-pig 47/37. Section of liver, showing fatty degeneration in the central vein area. (Sudan III stain) $\times 187$.

animals in the process of their elimination. It seems reasonable to conclude that in fifteen of the twenty-five animals the toxic material proved fatal.

The possibility of the effect being due to a virus must of course be considered, and this will be done in future experiments by animal transmission.

It is proposed to continue the investigation by using a further series of animals to confirm the results already obtained, using a filtrate the toxicity of which is standardized at least for each particular group of animals. Should the results be confirmed, the material should then be given by mouth, as much difference of opinion seems to exist on the danger of swallowing the constant discharge from chronic pyorrhœa.

I am greatly indebted to my colleagues in the John Hampton Hale laboratory, for helpful advice, particularly to Dr. Fish, Mr. Turner, and Dr. Maclean of St. Mary's Hospital. My thanks are also due to Mr. Hardwick and Mr. Ferguson of the Parodontal Clinic for providing the cases used, and to Sir William Willcox who confirmed the microscopic reports.

BIBLIOGRAPHY

- FISH, E. W., and MACLEAN, I., *Brit. Dent. J.*, 1936, **61**, 336.
WILLCOX, W., *Lancet*, 1931.

JOINT DISCUSSION No. 4

Section of Surgery and Section of Radiology

Chairman—G. GREY TURNER, M.S. (President, Section of Surgery)
in the Chair

[March 3, 1937]

DISCUSSION ON THE VALUE OF PRE- AND POST-
OPERATIVE IRRADIATION IN MALIGNANT DISEASE

Mr. W. Sampson Handley: There are not wanting sceptics who deny to X-radiation any value in connexion with operations for carcinoma. Their error is most clearly seen when we consider the value of post-operative radiation in the prevention of implantation recurrence. I have in mind three cases in which, subsequent to the removal of internal abdominal malignant growths, nodular lumps appeared in the abdominal wall.

The first case was that of an American woman who had a gastrectomy performed in Chicago for carcinoma. Some months after the operation a painless nodule appeared in the scar just above the umbilicus. It grew rather rapidly and ulcerated, but she appears to have taken no advice. When I saw her for the first time a prominent fungating circular mass, about eight inches in diameter, occupied the epigastric region. I judged it inoperable, though she had no visceral troubles, and no sign of visceral recurrence. She died a few months later after much suffering.

The second case was operated on by a colleague for a caecal carcinoma of low malignancy, with complete success. Five years later two nodules appeared in the abdominal scar and grew rather rapidly. They were treated two months ago by interstitial radium reinforced by deep X-rays. The nodules have shrunk, but it is too soon to estimate the final result.

The third case was a curious one, in which an acute appendicitis had infected a right malignant ovarian tumour. I removed the tumour and the appendix by a median hypogastric incision. Some months later after the wound had healed, a thickening, soon becoming nodular, appeared in the abdominal scar. It rapidly increased in size. After treatment by interstitial radium the lump shrank and disappeared, though a fibrotic thickening remains. The patient remains well two years after the treatment.

This short series of cases illustrates the reality of the danger of the implantation of floating cancer cells in an operation wound, the long latent period which may elapse before the recurrence, and the effectiveness of radium radiation in dealing with the condition. It may be inferred with absolute certainty that if radium can destroy massive implantation recurrences, it would *a fortiori*, if applied just after the operation, destroy the microscopic cancer cells which are the seed from which the recurrence grows. For this purpose deep X-rays would probably prove as effective as radium and more convenient.

The facts of implantation recurrence, even when they are considered alone, provide a wide field for the post-operative employment of deep X-rays. There are indeed few cases in which the possibility can be excluded. A short course of

deep X-rays should be applied to the scar after operation in all cases of gastric, intestinal, or pelvic malignant disease, as well as in breast cancer and in operations for malignant glands of the neck. Some surgeons in certain cases will prefer the insertion of radium tubes in the wound at the time of operation.

In regard to implantation recurrence, pre-operative radiation need hardly be considered, unless it is believed that pre-operative radiation can be made so effective that every cell in the growth is deprived of its power of proliferation. But in that case operation is superfluous. As a preventive of implantation post-operative radiation holds the field.

We now come to the crucial point of this discussion. Is it better, in cases in which doubt is felt as to whether operative removal of a disseminating growth can be made complete, to apply supplementary radiation before or after operation. I refer mainly to cancer of the breast. In dealing with the problem I am met by the difficulty that I have never advised pre-operative radiation, except in rare cases as a possible means of converting a fixed inoperable growth into a mobile one.

I must admit that my decision against pre-operative radiation is based on *a priori* grounds and may be considered a prejudice. My reasons are as follows: Pre-operative radiation involves unnecessary and undesirable delay in the performance of the operation. During the time of waiting the deep microscopic extensions of the growth which are its most dangerous part have time to make further advance. I believe some who practice the method postpone the operation for as long as three months. The delay would not matter if it were certain that meantime these deep extensions are kept inactive by the radiation treatment. But the evidence is the other way. In cases treated by X-rays only it is my experience that as a rule, while the primary growth shrinks and becomes mobile, dissemination proceeds unchecked.

It is certainly very difficult, even with modern apparatus and methods, to convey to any considerable depth beneath the skin a dose of X-radiation lethal to carcinoma cells. To attempt the irradiation of carcinoma cells in the pectoral fascia or in the pectoral muscle, through the whole thickness of a voluminous mamma is to impose an extreme handicap. But when the breast has been removed even deeper layers, such as the intercostal muscles or the pleura, are brought within a short distance of the skin, and exposed to the full force of the radiation. Certain of the glands, namely the apical glands of the axilla and the internal mammary glands, are so sheltered that I doubt whether they can be dealt with by any dose of X-rays that the overlying skin can tolerate. But the apical glands can be removed, and the internal mammary glands can be treated at the time of operation by interstitial radium tubes.

No proof has yet been supplied that X-radiation is able to destroy carcinoma cells in the internal mammary glands. I have supplied proof that interstitial radium is competent for the purpose. Even in advanced cases with sternal prominence and softening, and parasternal nodules in the intercostal muscles, interstitial radium may be successful. I show the patient in one such case, well—twelve years after interstitial radium treatment.

Beatson in Glasgow, and Hugh Lett in London, found occasional benefit, in cases of breast cancer, from oophorectomy. Now that a functional oophorectomy can be carried out by X-radiation, Grantley Taylor considers that a further trial of the effects of radiation castration should be made. The suggestion does not appear hopeful, since Ahlbom in 163 cases of breast cancer sterilized at the Radiumhemmet concludes that radiation-castration combined with local radiation therapy is no more advantageous than local radiation alone. It is often forgotten that breast cancer occurs more frequently after the menopause than before. The only real advantage of castration is that subsequent pregnancy is prevented; this end is more easily attained by contraceptive methods. There is no doubt that subsequent pregnancy is very dangerous; Trout states that out of 15 cases of pregnancy subsequent to breast cancer, 13 cases promptly developed carcinoma in the remaining breast.

F. E. Adair and F. W. Stewart at the Memorial Hospital have made a careful attempt to determine the value of pre-operative radiation in operable cases. In from two to three months operation followed and the specimen was carefully examined. Thirty-nine cases were subjected to radiation from a radium pack containing 4 gm. at a distance from the skin of 6 cm., using five ports. The dose was from 20,000 to 44,000 M.C.H. per port. In 28 per cent. of cases the tumour was found to have completely disappeared, and in 13 per cent. no growth was found in the glands. Viable cancer was still present in the breast in 28 per cent. and in the glands in 73 per cent. of cases. The authors hope, by introducing right along the line of the axillary vein a catheter containing a continuous line of radium tubes, to improve their results. Forty-two cases received pre-operative treatment by 200 kv. X-rays. Operation showed that the growth in the breast had been destroyed in 16.5 per cent., but in no case was the growth in the glands destroyed. Active viable growth remained in the breast in 43 per cent. of cases, and in the axillary glands in 100 per cent. of cases.

Dr. W. M. Levitt: I propose, in the first instance, to state the case for the combination of surgery with radiations in the treatment of carcinoma of the breast, for it is in this condition that the question of a combination of the two methods of treatment most frequently arises. Secondly, I shall discuss the questions that arise when the two methods are combined—such as the sequence in which they should be applied and the length of interval between them. Finally, I shall try to give an analysis of the practice with reference to these questions in certain leading foreign clinics.

Let us, first of all, consider the operable case. The value of surgery alone at this stage is now fairly accurately known, and few who have observed the results of modern deep X-ray and radium therapy would deny that these methods also have a certain value. The results of radium therapy alone in primary carcinoma of the breast have been published by Keynes and others, and they are sufficiently well known. Comparable results of deep X-ray therapy alone are not so easy to assess, since so few cases are sent for this form of treatment in an operable stage. However, results in inoperable cases and in post-operative recurrences place it beyond question that X-ray therapy can secure a percentage of five-year results. Thus, in a small series of cases of post-operative recurrences treated at St. Bartholomew's Hospital, 22% of the patients were alive and well five years after treatment, while in a recent address by Holfelder to this Section,¹ a slightly higher figure was reported in a much larger series of cases. Surgery alone, and radiations alone, are therefore each capable of providing some successes when used in the treatment of carcinoma of the breast. A different set of women would, however, be saved by the operative treatment from that which would be saved by radiation treatment, for the factors which make for radio-sensitivity and operative success, respectively, are widely different, and even in some respects antagonistic. The factors determining operability might be termed mainly mechanical, and if the disposition of the cells is sufficiently favourable, the patient will be cured by operation, however radio-resistant the growth may be. Radio-sensitivity, on the other hand, depends upon certain obscure biological properties in the cell, and many a radio-sensitive growth can be eradicated by irradiation, even though completely inoperable.

Let us assume that we combine our two methods of treatment—surgery and radiations. We next have to decide *how* we are to combine them: Should the irradiation precede or follow the operation? How long is to be allowed to elapse after the one and before the other? What modifications are to be made in the techniques of each? What are the dangers? and, finally, should X-rays or radium be used in the irradiation?

¹ Section of Radiology, November 20, 1936, *Proceedings*, 30, 773.

In the past it has been the common practice to carry out the radical operation first, and to regard the X-ray therapy as a rather doubtful safeguard following the operation. Often, encouraged perhaps by the surgeon, the radiologist has fallen into the error of being satisfied with a much less thorough irradiation than he would have given in a case with definitely appreciable disease. Clearly this is bad practice, since the carcinoma cell requires a lethal dose of radiations, whether it is living in small colonies which have escaped the surgeon's knife, or in large colonies which are clinically appreciable. Moreover, it has to be distributed to just as wide an area, since the chest wall and all the glandular areas on that side require to be dealt with. With modern methods of deep X-ray therapy, the general condition of the patient does not suffer severely, even with the thorough irradiation advocated, and the effect on the blood-count is almost negligible. Partly because of the tendency in the past to under-treatment in these cases, post-operative irradiation has not so far produced any very spectacular improvement in the published results, although there is little doubt that the percentage of local recurrences is materially decreased. Another factor which has adversely influenced the results in post-operative series of cases, is that few surgeons send their patients for irradiation as a routine measure, but only when it is believed that the operation has not succeeded in removing all the disease.

The surgeon is usually found to favour post-operative irradiation, and his objections to pre-operative irradiation have been presented by Mr. Sampson Handley. There is, first of all, undesirable postponement of the operation. It is true that the irradiation does entail postponement of the operation for from four to six weeks. Secondly, it is true that the progress of secondary deposits is uninfluenced by local irradiation. But it is equally true that the progress of secondary deposits is uninfluenced by immediate surgery. The question is, whether the radiation treatment is capable of preventing the occurrence of *fresh* secondaries, and if so, at what stage in the treatment it becomes effective in doing this. It is probable that the treatment is so effective, and that this stage is reached in about a fortnight after the beginning of the radiation treatment; and surely the danger to the patient during this fortnight must at least be offset by the reduced danger of implantation and dissemination at the operation. Another objection—that it is difficult to convey an adequate dose to any considerable depth beneath the skin without risk to the normal tissues—does not hold in so far as high-voltage therapy is concerned, since the same dose can safely be delivered, at any required depth, as can be tolerated by the skin. The objection that deep X-rays may lower the vitality is to some extent true, but when high voltage rays are used, the difficulty of the operation is not seriously increased. Finally, the objection that the internal mammary and apical axillary glands cannot be adequately irradiated does not hold when hard, i.e. high-voltage, rays are used, since these rays pass through bone almost as readily as they do through the softer tissues, and adequate deep dosage is easily obtained. In favour of pre-operative irradiation, we have also to consider the fact that there is definite experimental evidence, not only that the irradiated carcinoma cells are much less likely to flourish if implanted in a new site at the operation, but also that carcinoma cells are much less likely to take root when implanted into irradiated tissue. Moreover, clinical observation shows that in the majority of cases considerable reduction in the size of the growth follows the irradiation, and this must clearly be interpreted as damage to the tumour cells. It is, however, a curious fact that although in many cases microscopical examination of a previously irradiated growth shows obvious radiation injury, in other cases large tracts of carcinoma cells may be apparently unaffected. Holfelder has recently adduced some evidence to show that the X-ray damage affects principally the genes of the nucleus, and that although the cell irradiated may continue to live an apparently normal life, it is still incapable of reproduction. In this way, the well-known delayed effect of radiations may be accounted for.

It will be seen that there is a strong case for pre-operative irradiation. The surgeon will still, however, want to know whether it is safe to operate in a region which has been previously more or less heavily irradiated. It cannot be denied that with maximum X-ray dosage preceding the operation, a number of disasters have occurred, mainly due to sepsis, and in order to render the method safe, some reduction in radiation dosage is necessary. This deficiency in dosage should, however, be made up by a supplementary course of radiation treatment as soon as the patient has sufficiently recovered from the operation. This, as we shall see, has become the practice in certain leading foreign clinics, and experience has shown that the method is safe, and that healing occurs satisfactorily after the operation.

The next question is as to the interval between the irradiation and the operation, and vice versa.

In the case of post-operative irradiation only, the sooner the irradiation is begun the better. In a number of cases treated at St. Bartholomew's Hospital, X-ray treatment has been applied as early as the second or third day after the operation, without any untoward result being observed. As a rule, however, it is better to wait until the stitches have been removed.

When pre-operative treatment is being given, the operation should be carried out either immediately after the completion of the irradiation, so that healing may be well under way before the stage of reaction from the rays is reached, or from four to six weeks after the completion of the irradiation, i.e. after the X-ray reaction has subsided. The latter interval, four to six weeks, is that most usually selected. For the supplementary post-operative course an interval of two or three weeks may be allowed.

As regards the modifications in technique, the reduction of dosage in the pre-operative irradiation and its compensation by a supplementary post-operative course have already been mentioned. It has not been found that any modification is called for in the radical operation, provided that undue tension on the stitches is avoided. The use of the diathermy knife in the operation does not appear to increase the risks.

Finally, we have to consider whether X-rays or radium should be used in the irradiation. When post-operative irradiation only is being considered, there is scarcely a choice, since the field is unsuitable for interstitial radium; and as between X-ray therapy and any form of surface radium, there can be no question that X-ray therapy offers the most satisfactory means of applying an adequate and uniform irradiation to the wide area necessary, while ensuring protection of the deeper structures. With modern methods of deep X-ray therapy, protection of internal structures is easily obtained by tangential methods of treatment.

With regard to pre-operative irradiation, I do not think it matters much whether this is carried out by interstitial radium or by deep X-ray therapy. It is probable that a better irradiation of the apex of the axilla and supraclavicular region, and especially of the region behind the clavicle, is afforded by X-rays. Another point in favour of X-rays is that the administration of an anæsthetic is avoided, but it must be remembered that the X-ray treatment is more tedious, in that it requires about three weeks to complete.

I have dealt mainly with operable carcinoma of the breast, because it is here that the problem of pre- and post-operative irradiation most frequently arises. In cases of inoperable carcinoma of the breast, it frequently happens that X-ray treatment, not intended as a pre-operative irradiation, leads to such a satisfactory result that the condition becomes operable. In such cases, irradiation has been carried out with full dosage, and the radiologist is frequently asked whether it is safe to operate. The answer is that it is perfectly safe, so long as a complete radical operation is not attempted. I have already referred to the fact that sepsis is a complication in the radical operation in a certain number of cases in which pre-operative irradiation has

been carried out with full dosage. In my opinion, local removal of the breast is of great value in these cases following X-ray treatment, and it should be undertaken wherever possible, even if the growth has completely disappeared as a result of the X-ray treatment and the patient appears to be perfectly well. A breast which has once been the site of a carcinoma always remains a menace to the patient, whether it has been successfully treated by X-rays or by radium.

The general principles of the combination of surgery with radiations that have been discussed in connexion with carcinoma of the breast apply equally to malignant disease in other sites—excluding, however, radio-resistant growths such as carcinoma of the bowel, and fibrosarcoma. There is one group of malignant disease, however, to which I should particularly like to refer—that of the retroperitoneal growths of infancy and childhood. These, whether arising from the kidney or some other site, are nearly always radio-sensitive. Even hopelessly inoperable growths may often be rendered operable by X-ray treatment, and in many instances growths of moderate size apparently completely disappear. I would strongly urge that pre-operative irradiation should be carried out in these cases, not only because it reduces the size of the growth and thereby renders operation easier, but also because the risk of dissemination at the operation is almost certainly markedly decreased. Supplementary post-operative irradiation should be given in the same way as for carcinoma of the breast.

I will conclude with a table in which I have attempted to give an analysis of the method of treatment of carcinoma of the breast in certain leading foreign clinics, and I should like here to acknowledge my indebtedness to Dr. Coutard of Paris, Professor Holfelder of Frankfurt-on-Main, Professor Berven of Stockholm, and Professor Holthusen of Hamburg, for their kindness and courtesy in replying to my inquiries and in filling up a tiresome questionnaire.

	COUTARD (Paris)	HOLFELDER (Frankfurt a M)	BERVEN (Stockholm)	HOLTHUSEN (Hamburg)
Method of treatment	For very radio-sensitive growths—irradiation alone For other growths, if operable—irradiation and surgery	For Stage I and IIa Steinthal-surgery and irradiation For Stage IIb and c and Stage III Steinthal - irradiation alone	For Stage I and II Steinthal-irradiation and surgery For Stage III Steinthal-irradiation alone	For operable cases—operation and irradiation For inoperable cases—irradiation alone
X-rays or radium	Not stated	X-rays	X-rays	For extensive areas—X-rays For localized growths—radium
Pre- or post-operative irradiation or both?	Pre-operative only	Pre- and post-operative	Pre- and post-operative	Post-operative only
Optimum interval between operation and irradiation or vice versa	Before 25th day	Pre-operative 10 to 12 weeks Post-operative 2 to 3 weeks	Pre-operative 3 to 4 weeks Post-operative 1 week	Up to 4 weeks
? modification of operation or irradiation when combined	Not stated	None	Sub-maximal dose in pre-operative series Supplementary post-operative series	Very prolonged irradiation—three series at intervals of 6 weeks

Dr. George F. Stebbing: The considerations which should guide us in pre- and post-operation irradiation are perhaps best illustrated by considering carcinoma of the breast.

In my own practice I always begin the treatment of these cases on the assumption that by irradiation alone I shall be able to get rid of the tumour. The irradiation is planned to this end, and an excision of the breast and adjacent structures is only

performed when it has been realized that irradiation by itself is not going to be successful.

If, when the patient is first seen, it is decided that operation is to be performed, pre-operative irradiation can be given for the following purposes :—

(1) To reduce the size of the tumour by getting rid of those cells which are most radio-sensitive.

(2) To render the tumour more mobile, that is, to reduce the amount of infiltration, both neoplastic and inflammatory, in the tissues surrounding the tumour.

(3) To lessen the vitality of all the tumour cells, so that if during the operation any of them are sewn on to the surface of the wound, or squeezed into the lymphatic stream, there is less chance of their surviving to form local recurrences or distant metastases.

It is difficult to decide how much irradiation should be given before operation, for the purposes enumerated above to be best served. In the majority of tumours there are a certain number of very radio-sensitive cells and a very small dose of X-rays is therefore better than none, but it is wiser to give such a dose of X-rays as will kill off all those tumour cells which can be got rid of without any lasting damage to the normal surrounding structures. In the absence of a radium beam, this is best done by means of X-rays. The actual technique employed is capable of many variations, but it may be said, generally, that using 200 kv. and a Thoraeus filter, some 4,500 r should be delivered within three weeks to every part of the patient which is assumed to contain carcinoma cells. After such an irradiation there will be a reaction of the skin which will make it necessary to postpone the operation for about another three weeks, but by the end of that time a radical operation may be performed. The healing of the operation wound after such irradiation is definitely slower than if there had been no irradiation, and if so much skin has been removed as to leave an open wound, an immediate skin-graft will not take, granulations will not form for a long time, and it is generally advisable to postpone secondary grafting for about two months.

Post-operative irradiation is only given on the assumption that the operation has left some tumour cells behind it, and it is necessary to decide where such tumour cells may be before it is possible to treat them by irradiation. It is generally assumed that tumour cells sewn on the wound surface during the operation would be more rapidly destroyed than cells growing in a tumour. This is unlikely to be true, for cells that are in a resting-state and cells that are partially asphyxiated are more radio-resistant than cells forming a part of a growing tumour, and there is no reason to believe that a small, even microscopic deposit, requires less irradiation to kill it than a large one. The only important thing is that each cell of the tumour, whether large or small, must receive the necessary amount of irradiation in the proper time. After a radical operation for the breast it is not possible to deliver to that part of the wound over the chest-wall, which may be the seat of insemination, an effective carcinoma-killing dose of irradiation without doing lasting injury to the skin, and especially is this true when an extensive skin removal has been necessary, with resulting cicatricial changes in the skin and subcutaneous tissue.

For these reasons I very much doubt whether it is desirable to give any routine post-operative irradiation to the site of the breast, epigastrium, or lateral aspect of the chest-wall. Such irradiation is likely to stop short of anything that can be really effective, and yet may make it impossible to treat by irradiation any recurrence of the growth. If, or when, there are such recurrences in this area, they can be treated easily and successfully by radium, which causes little constitutional disturbance to the patient and can be confined to the immediate neighbourhood of the recurrence.

The position is different, however, with regard to the axilla. The glands at the apex of the axilla and in the supraclavicular region are difficult to eradicate completely and are a not-uncommon site of recurrence of the growth. Both these

regions can be effectually irradiated, i.e. irradiation can be so arranged that every lymph-gland in these regions can receive a carcinoma-killing dose without causing more than a temporary inconvenience to the patient. This I think should be done for every patient after operation for carcinoma of the breast, and it is an advantage for it to be done as soon as possible, there being no need to wait until the wound has healed before the irradiation is commenced.

The problem of retrosternal and internal mammary glands has not yet been solved. To plant radium tubes at the inner ends of the intercostal spaces after operation is a hit-or-miss method, of very doubtful efficacy, but may be used on the grounds that if it often misses and sometimes hits it may be worth while. If such a method is employed it is desirable that iso-dose curves representing the intensity of the field of irradiation round such tubes should be carefully considered, and tubes of such size and strength should be used that a dose of not less than 6,000 r should be delivered at the distance from the tubes which the internal mammary glands are assumed to be.

In speaking of irradiation, I have not drawn any distinction between X-rays and radium. If large enough quantities of radium are available, probably the best results would be obtained by using a radium beam for the whole of this work, but in the present circumstances it is necessary to use X-rays for all those cases in which it is assumed the tumour cells are deeper than about 1 cm. from the surface. For very superficial tumours, such as local recurrences after operation, applications at a few millimetres from the surface form the best means of treatment, with little discomfort to the patient.

I have tried to speak on the general subject of pre- and post-operative irradiation for carcinoma of the breast, but even in this part of the body it will often be found that if an effective pre-operative irradiation is given, the whole tumour will entirely disappear before the operation is undertaken. This is particularly true in rapidly-growing ill-defined tumours in young women, and I think it unlikely that removal of such a breast is of any benefit to the patient. Many such patients will return with many metastases in different parts of the body, and never show any signs of recurrence of the local tumour.

The principles that I have laid down are applicable to all parts of the body other than the breast. Whenever it is proposed to remove a carcinoma, adequate irradiation before the operation is likely to prevent local recurrences and to lessen the likelihood of metastases being caused by the operation itself. Post-operative irradiation should always be employed where it is known or assumed that carcinoma cells have been left behind, and the amount given must be the full dose which we know is necessary to get rid of carcinoma.

Suspected metastases, even at a distance from the primary site, should always be treated when they are accessible to irradiation and not so numerous as to render the effective treatment of all of them impossible. I would, however, urge that no attempt be made to treat the patient before metastases are suspected, with the idea of preventing their occurrence. There is no such thing as "prophylactic" irradiation. I should very much like to see the term "prophylactic" in connexion with irradiation completely abolished. Its use is misleading and frequently gives rise to a patient receiving inadequate treatment, or treatment to an area that should be left alone until there is evidence of malignant disease there.

Section of the History of Medicine

President—E. W. GOODALL, O.B.E., M.D.

[April 7, 1937]

Notes on Some Landmarks in Tropical Medicine

By P. H. MANSON-BAHR, D.S.O., M.D., F.R.C.P.

PATRICK MANSON (1844–1922) is justly regarded as the father of modern tropical medicine. He was born of Scottish parents in the township of Old Meldrum, Aberdeenshire and educated at Aberdeen University. At 22 he migrated to Formosa, later moving on to Amoy in Southern China. Altogether he lived twenty-three years in China, practising latterly in Hong Kong for seven years.

In Amoy in 1877 he made his first momentous discovery of filarial periodicity. The filarial embryo had been demonstrated by Timothy Lewis (1841–1886), some five years previously, but it was left to Manson to point out the true implication of its appearance in the blood-stream at night-time only, and the bearing of this phenomenon upon the life-history of the parasite. He argued then, that this was a habit-adaptation to that of the night-feeding brown mosquito of Amoy (*Culex pipiens*). In 1879 he proved this. He found that the mosquito served in the capacity of a "nurse", or what is now known as an intermediary host. The filaria underwent development in the thoracic muscles of this insect, becoming completely changed in appearance during this process.

Amongst Manson's relics at his death was a letter from Timothy Lewis, dated January 14, 1878, expressing his appreciation of Manson's communications, but warning him against unhesitatingly regarding the minute filariae he had found in the tissues of the mosquito as developmental stages, as they might prove to be special nematode parasites peculiar to these insects (a fact which is now known to be true). Lewis, however, judging by his own personal dissection of mosquitoes, could find no morphological differences between them and the embryo of *Filaria sanguinis hominis*.

Lewis was shortly after recalled to Netley, where he organized the pathological department there and did signal service. He was also closely associated with D. D. Cunningham (1843–1914), the discoverer of *Entamoeba coli*, as well as of the parasite of oriental sore, which he recognized, but did not name.

Manson was in correspondence with T. Spencer Cobbold (1828–1886), who as the most distinguished helminthologist of his time, was the recipient of specimens collected all over the world. It was Cobbold who named *Filaria bancrofti*, *Bilharzia hæmatobia*, and many other parasites. His appointments were curiously diverse: he was working at geology in the British Museum, and at parasitology at the Middlesex Hospital, as well as at the Veterinary College. It was his privilege to present Manson's communications to the Linnean Society and to the Quekett Microscopical Club. Hence the following story:—

On June 20, 1879, Manson wrote to Cobbold an account of his experiments and forwarded him filaria-impregnated mosquitoes preserved in glycerine and fed on the

blood of his Chinese gardener, who was heavily infected. There were five glass bottles filled with specimens and adequately labelled. The letter ends as follows :—

“It seems to me that Lewis by his great discovery has opened a new field in tropical pathology. Men like myself, in general practice, are but poor and very slow investigators, crippled as we are, with the necessity of making our daily bread.”

These were evidently the specimens which were demonstrated by Cobbold to the Medical Society of Middlesex Hospital in February 1884, before a large audience. The leather case containing these mosquitoes intact, just as they left Amoy in 1879, was rediscovered in the Royal College of Surgeons by Prof. R. T. Leiper, in 1935.¹

Manson in later years (1895), being in need of some infected mosquitoes, ransacked London for them in vain. In a letter to Ronald Ross, on December 23, 1895, he wrote :—

“I have at last succeeded in getting a filariated mosquito. Many years ago—seventeen or eighteen—I sent to Cobbold a lot of filariated mosquitoes. I knew that Cobbold’s collection had gone to the College of Surgeons, and so got permission to look over them for my mosquitoes, but failing, I went to Stephen Mackenzie, and there found a small bottle with a solitary mosquito floating in glycerine. In a section of the blood in its abdomen there were my Amoy filariae, and in its thoracic muscles they were too, most beautiful to behold.”

This was evidently one insect of this batch which has been so dramatically rediscovered.

Joseph Bancroft (1836-1894), the discoverer of the adult form, *Filaria bancrofti* (so-named by Cobbold) was an Englishman who settled in Brisbane in 1864. He never communicated directly with Manson, though his son, Thomas Bancroft, in 1899, consigned to Manson infected mosquitoes preserved in glycerine, and these were the insects which were sectioned in celloidin by Dr. G. Carmichael Low in the following year, whereby the complete life-history of the larva was unfolded and its presence in the proboscis of the insect demonstrated. This showed that the mosquito conveyed the parasite in the act of biting—a mode of communication which had been suggested by Cobbold himself in a review in the *Veterinarian* as far back as March 1883, though somehow or other, this suggestion had not been acted upon. We do know, however, that the elder Bancroft, writing to Cobbold in the spring of 1877, expressed his belief that mosquitoes would be found to convey filariasis, but his own examinations had proved entirely inconclusive in that direction.

It is fortunate for posterity that Manson kept a scientific diary (now preserved in Manson House) commencing in June 1877 and continuing to 1896. It consists of 615 closely written pages and contains an account of his major discoveries, and from it many historical data have been culled. In 1887 Manson visited Li Hung Chang, who was said to be suffering from cancer of the tongue. Luckily it was only a sublingual abscess, which was successfully opened. On returning he received this gracious letter from the great statesman.

“Li Hung Chang to Patrick Manson.

4th December, 1887.

“On account of a recent slight malady at the root of my tongue I have had the honour to receive your visit from afar. My thanks I am unable to express, and your treatment has already resulted in a complete cure. Calm, then, your anxiety on my account. I send you enclosed a photograph which may perhaps

¹ The actual specimen was exhibited at the meeting.

serve as a reminder of the sincerity of our good feelings towards one another ; and I hope you will accept it. This is the object of my letter and I take this opportunity of wishing you an elegant time. My card is enclosed.

Kuang Hsii, 13th year, 10th moon and 20th day."

The story of the discovery of the lung fluke—*Paragonimus westermanii* (then designated by Cobbold *Distoma Ringeri*)—is also a romance and is related in the *Diary*. On April 24, 1878 a mandarin consulted Manson on account of some eczematous eruption, but, whilst speaking, he hawked up a small quantity of reddish sputum and it was noted that his voice was rough and loud. Observing that the sputum was tinged with blood, Manson immediately seized a portion with his forceps and put it under his primitive microscope to look for filariæ (which he then believed sought to leave the body by this route) but he was surprised to find eggs of a hitherto undiscovered parasite. Immediately he communicated his discovery to Dr. Ringer, a correspondent in Formosa, and besought him to investigate a Portuguese patient who, suffering from a thoracic aneurism, had left Amoy Hospital and returned to Formosa. At the autopsy on this man Dr. Ringer found a parasite, the size of a pea, in the lung and forwarded it in spirit to Manson, who was delighted to observe in the sediment of the bottle, ova similar to those in the sputum of the Chinese patient already noted. The parent worm was then sent to Cobbold who recognized it as a new species and named it *Distoma Ringeri*.

Later Manson made observations on these eggs, kept for various periods in water in order to elucidate their life-history. He was able to observe, after many weeks, the liberation of the miracidium, and made several shrewd guesses at its life-history which, however, was not fully worked out till thirty-five years later by Nakagawa.

The first intermediary of *Paragonimus* is now known to be a freshwater mollusc—*Melania libertina* (Gould), and yet we find in the *Diary* a letter from a conchologist, R. Hungerford, dated October 21, 1881, suggesting that this snail acted as carrier in the transmission of this trematode. No further notice of this pregnant suggestion appears to have been made at this time, and a valuable hypothesis remained abortive.

The most amazing part of these fundamental discoveries is that they were made without any recourse to post-mortem material. Thus we find Manson writing :—

"The difficulties of obtaining post-mortem examinations were insuperable. One of my filaria patients was dying of an intercurrent disease. Being eager to find the parental form, I offered him 200 dollars to be handed to his widow for permission to perform a post-mortem dissection of his body. He agreed and a proper document was drawn up. On his death the widow claimed the money and I was allowed to dissect the body. My brother and I proceeded to the man's house in the very heart of the native town, prepared to spend several hours in search of the parental filaria (which had then not been discovered). I had barely commenced the section when we heard an ominous noise outside. A mob had gathered and was anxious to know what the 'foreign devils' were doing. We had to run for our lives, and I lost my two hundred dollars. Being denied the opportunity of necropsies in man, I had to make use of dogs, cats, and birds of various sorts. In the course of these examinations a great variety of hæmatozoal parasites were found. I had found that the blood of the magpie contained at least two species of filaria, so I procured as many of these birds as possible, but the Chinese told me I must stop my work in this direction, because the magpie is a sacred bird in China, tradition holding that, many years ago, the spirit of a defunct Emperor had entered one of these birds. Therefore it was possible that either I, or my friends, might shoot this particular fowl. I don't know that this absolutely deterred me, but the birds themselves

which, under ordinary circumstances, are remarkably tame in China, soon got to know that I was after them."

Manson's part in the mosquito malaria hypothesis, as it was then called, is so well known that it hardly bears repetition. Manson's long connexion with Ronald Ross commenced in April 1894 in London and their original correspondence is preserved *in toto*. The first letter from Manson to Ross is dated April 9, 1894, and in it he explains to his pupil that the reason why he has not recognized the malaria parasite is because he has not used the proper technique.

The debt Ross owed to Manson was expressed in 1898 when he wrote :—

"These observations prove the mosquito theory, as expounded by Dr. Patrick Manson, and in conclusion, I should add that I have consistently received the benefit of his advice during the enquiry. His brilliant instruction so accurately indicated the true line of research that it has been my part merely to follow its direction."

Finally, Manson's maxim of research should be engraved on the walls of every scientific laboratory. It runs as follows :—

"Never refuse to see what you do not want to see, or what might go against your own cherished hypothesis, or against the view of authorities. These are just the clues to follow up, as is also, and emphatically so, the thing you have never seen or heard of before. The thing you cannot get a pigeon-hole for is the finger-point showing the way to discovery."

Section for the Study of Disease in Children

President—C. PAGET LAPAGE, M.D.

[May 28, 1937]

Tumour of the Spinal Cord in a Child aged 2½ years : Specimens.—C. P. LAPAGE, M.D., and D. S. POOLE WILSON, M.S. (introduced by Dr. LAPAGE).

D. L. H., female, aged 2½ years. Full-term baby ; instrumental delivery.

History of present illness.—Sent by Dr. Pearce of Walkden, to the Royal Manchester Children's Hospital, January 15, 1937. The mother said that for several days the child had been listless and fretful, not taking any food, and crying if touched or picked up. She was now unable to walk and for two days had been fed on brandy and water. Three weeks previously she had fallen downstairs and hurt her back. The injury was apparently not severe and no further attention was paid to it at the time. Following the accident the child was able to run about and play as usual. Previous to the accident she had not been well ; four months before she had suffered from pain in one arm ; the mother had attributed this to rheumatism.

The following further information was obtained from the mother after the autopsy. During October 1936 the child complained of pain in the left hand and did not like it to be touched. This pain disappeared for a time but subsequently returned, and the mother noticed that the left hand was not used, and that the arm hung by the side. She took the child to a hospital, and, after a negative X-ray examination, was informed that the trouble was due to rheumatism. Some degree of movement was always present in the arm.

On examination.—The child lay quietly when not disturbed, but resented examination. The pupils were equal and small, and reacted to light. The face was turned to the left with the chin pointing upwards, and was held rigidly in this position. All cervical movements were equally poor. No bony deformity of the cervical spine was palpable either externally or through the mouth. There were no abnormal glandular swellings. The arms lay slightly abducted at the shoulders, flexed at the elbows and with the forearms pronated. There appeared to be some degree of movement in all muscle groups except those of the pectoral girdle. The biceps jerk was present on either side ; the triceps jerk absent. The legs were rather spastic, but movement was observed in all the main muscle groups. Knee-jerks active ; plantar responses flexor. Radiological examination : The cervical and thoracic vertebræ showed no evidence of dislocation, fracture or other diseases.

Progress.—The signs of spinal compression became progressively more marked. Complete paraplegia and loss of sphincteric control ensued. Death occurred on the ninth day following an attack of hyperpyrexia.

Autopsy findings.—On external examination no deformity or undue mobility of the cervical spine was found. Subsequent examination showed no evidence of a fracture or dislocation of the cervical or thoracic vertebræ. The dura mater

enclosing the spinal cord appeared normal. A tumour, 1 cm. in diameter, was found in the extradural course of the seventh left cervical nerve and this communicated through the intervertebral foramina with a further swelling, 1.5 cm. in diameter, in the extravertebral course of the nerve. The whole gave the macroscopic appearance of an hour-glass or dumb-bell neuroma.

On its posterior aspect the spinal cord was covered with multiple small ecchymoses, which extended from the level of the fifth cervical segment downwards. There was no gross subarachnoid hæmorrhage. A tumour, 5 cm. long, 1.4 cm. broad, and 0.8 cm. thick, lay on the anterior aspect of the cord, apparently being situated between it and the arachnoid membrane (fig. 1). It extended in length from the fourth



FIG. 1.—The dura mater has been divided longitudinally to show the tumour, with its smooth and rounded upper extremity, lying on the anterior aspect of the spinal cord.

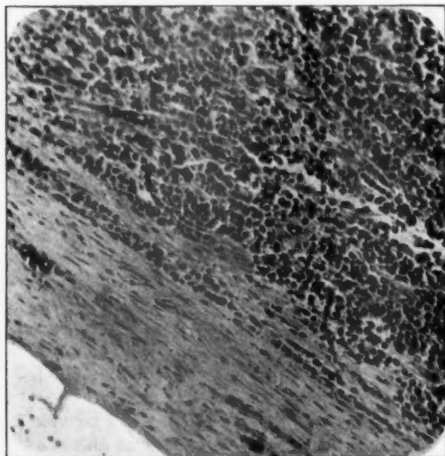


FIG. 2.—Section of tumour lying on the outer aspect of the pia mater. $\times 150$.

cervical to the fifth thoracic segment. The cord was compressed by this tumour, which was embraced by the nerve-roots running forwards to reach the intervertebral foramina. The dura at the point of emergence of the seventh left cervical nerve was not expanded, the intradural and extradural tumours, if communicating, being joined by a constricted portion.

Pathological report.—(Dr. W. Susman). The growth lying over the spinal cord is distinct from it and appears to be essentially in the pia-arachnoid although some extension under the pia has occurred (fig. 2). The growth has extended along and

into many nerves especially in the ventral surface of the cord (fig. 3), but has not invaded the cord itself. Pressure by the growth has given rise to degeneration chiefly in the posterior and antero-lateral columns of the cord.

In histological appearance all the specimens are similar. The growth is cellular, and made up of polyhedral cells in masses of varying sizes, and in strands. At

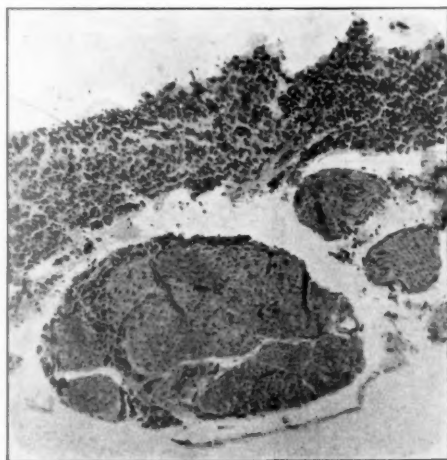


FIG. 3.—Section showing the invasion of the nerves lying on the ventral surface of the cord by the tumour. $\times 80$.

times this tends to form into circular structures. Occasionally the cells approach the columnar type. Mitotic figures are present. There is an appreciable amount of necrosis, and some hæmorrhage. The histological features are those of a malignant ependymoma of the spinal cord.

Dr. LAPAGE said that when he first saw the case he thought it might be one of spontaneous inflammatory dislocation of the atlanto-axial joint. The child was, however, too ill for many investigations, and a previous history of pain in the arm had not been forthcoming. In his previous cases of spinal tumour, pain radiating from the nerve-roots had always been a very prominent feature.

Craniofacial Dysostosis (Crouzon's Syndrome).—R. W. B. ELLIS, M.D.

A. H., a boy, aged 12, attended Guy's Hospital in February 1937, on account of unresolved pneumonia which has since cleared. The facial deformity has been noted since infancy, but the prominence of the eyes has become more marked recently, and the sight has become worse. There are three older children and one younger, all said to be normal, and one premature stillbirth. The father is normal but the mother shows a very slight degree of the same facial deformity and has a right external strabismus. The parents are unrelated.

On examination.—A well-developed and nourished boy with oxycephaly and bilateral flattening of the frontal region. There is extreme prominence and wide separation of the eyes, bilateral external strabismus, and congenital coloboma of

the irides. The upper lip is short and the palate high and arched. The eyesight is grossly defective.



Showing hypertelorism and coloboma of irides. Showing oxycephaly exophthalmos, and short upper lip.

Ophthalmic report (Mr. Law): Retinal veins engorged and tortuous. Both discs show a pathological pallor.

Radiological report (Mr. Worth): Evidence of oxycephaly. There is much convolutional marking of the inner table.

Cranial measurements (Mr. Whillis): Length 16.5 cm., breadth 13.5 cm., horizontal circumference 48.3 cm., facial length 11.2 cm., facial width 12.2 cm. Nasion toinion, 34.5 cm. Cephalic index 81.8.

Comment.—Characteristic features are the association of oxycephaly with exophthalmos, hypertelorism, optic atrophy, and high arched palate. Prognathism is less pronounced in this boy than in some of the published cases, but he shows the characteristic short upper lip. Coloboma of the irides is also a not infrequent associated finding. A number of such cases have been reported in this country (two having been shown recently before the Section of Ophthalmology, together with one example of Apert's acrocephalosyndactyly, by Mr. S. R. Gerstman (*Proc. Roy. Soc. Med.*, 1937, 30, 387), but in most instances they have been described simply as oxycephalic.

Dr. PARKES WEBER said he wondered whether Dr. Ellis regarded the less uncommon "turriform" type of forehead (German "Turmschädel") as a minor form of Crouzon's craniofacial dysostosis. It (the turriform type) was generally mentioned amongst the congenital abnormalities occasionally associated with hereditary hæmolytic jaundice. He believed that this association had been first noticed at Tübingen, where both these inherited abnormalities were relatively frequent, or at least not so rarely met with as in England.

Hypochromic Anæmia, Congenital Heart Disease, and Peculiar Facies.

—P. R. EVANS, M.B. (for WILFRID SHELDON, M.D.).

Male aged 11 months. Parents and sister well.

Full-term child; birth-weight 6 lb. Exomphalos operated on successfully two hours after birth. Systolic murmur and thrill noticed.

Fed on a variety of artificial foods—Nestlé's milk chiefly. Progressed slowly; has not lifted his head, sat, crawled, or spoken any words. Two teeth at 9 months. Goes blue in face when crying. Treated with thyroid, without improvement.

On examination.—Small child (weight $15\frac{1}{2}$ lb.). Head circumference $17\frac{1}{4}$ in., fontanelle 1 in. Hair glossy and fine. Coarse features, broad nasal bridge, rather large tongue. No nasal discharge. Eyes normal. Can see and hear. Grips objects; can sit for a short time. Two teeth erupted. Curvilinear dorso-lumbar kyphosis.

Heart enlarged to left. Systolic thrill over præcordium, systolic murmur widely audible but maximal up left border of sternum. Signs of emphysema of right lung and impaired air-entry into left.



Showing the peculiar facies, somewhat resembling that of gargoyism. Costal margin and spleen outlined.



Showing the dorso-lumbar kyphosis.

Umbilical hernia. Liver not enlarged. Spleen $2\frac{1}{2}$ fingerbreadths.

Blood: Wassermann reaction negative. Cholesterol 176 mgm. per 100 c.c. R.B.C. 5,670,000; Hb. 38%; C.I. 0.34. W.B.C. 7,000 (polys. 37%; eos. 3%; basos. 1%; lymphos. 58%; large monos. 1%).

X-ray examination.—Pituitary fossa small; lumbar spine normal; wrists normal; heart enlarged to left.

Discussion.—The PRESIDENT asked whether Dr. Evans would consider the diagnosis of Von Jaksch's anæmia, though the blood did not show the characteristic changes. The child's appearance was suggestive of blood disease and the splenic enlargement was

considerable and very like that seen in Von Jaksch's disease, being of a flat "pan-cake" like nature.

Dr. SHELDON said he thought that the anæmia in this case was nutritional, being due entirely to a low hæmoglobin level. Although the spleen was enlarged, the high red count and lack of myelocytes were points against a diagnosis of Von Jaksch's anæmia. The case had been brought before the Section, not on account of the anæmia, but because of the boy's peculiar facial appearance which was reminiscent of other cases which had been grouped together under the title of "gargoylism." Most of these patients had, at some time or other in their history, been regarded as either cretins or congenital syphilitics; in this particular case the Wassermann reaction was negative, and before the boy came to hospital he had already had a long course of thyroid without any benefit. Although the facial appearance was that of a gargoyle, and the mental deficiency and enlarged spleen were also features of that condition, the clinical picture was by no means complete, as the corneæ were clear, there was no deformity of the pituitary fossa, the liver was not enlarged, and there was no limitation of movement of any of the large joints.

Specimen of Congenital Genito-urinary Abnormalities with Suprarenal Enlargement.—P. R. EVANS, M.B. (for WILFRID SHELDON, M.D.).

Alan G., female, aged 7 weeks, second child of healthy parents who are not related by blood. Birth-weight 10½ lb. Breast fed for five weeks, then given half-cream Cow-and-Gate milk. Projectile vomiting began 11 days after birth, and occurred every day during the last fortnight of life. Constipation for three days before death. 7.5.37: Had two convulsions. Admitted to hospital.

On examination.—Temperature 94° F.; pulse 112; respirations irregular, infrequent and gasping. Collapsed. Fontanelle depressed but skin elastic. Genitalia (fig. 1):

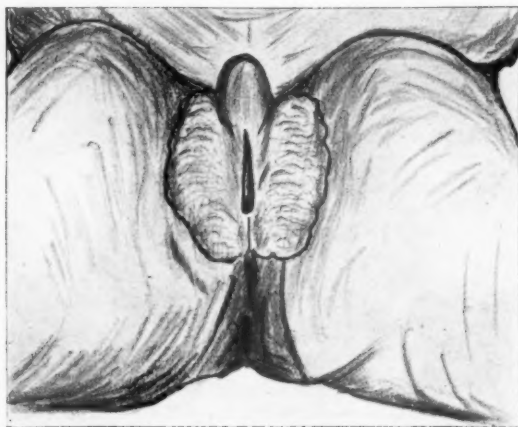


FIG. 1.—External genitalia, showing large clitoris without prepuce, cleft running back to urethral opening, and wrinkled labial skin.

Clitoris 2 cm. in length and 1 cm. in diameter; labia consisted of loose wrinkled skin similar to infantile scrotal skin; no vaginal orifice. A fissure ran back from the undersurface of the clitoris to the urethral orifice, which was situated in the anterior part of the perineum.

Glucose-saline was given by mouth and the patient was warmed. Temperature rose to 100° F. On catheterization, 2 c.c. urine obtained; occasional pus cell seen; albumin ++, Fehling's test +, Rothera's test negative.

Subcutaneous glucose-saline was given, but death occurred a few hours later.

Post-mortem findings.—(Permission given for incomplete examination only.)—Suprarenals large. Horse-shoe kidney. Urethra showed a well-developed verumontanum; below this an opening 2 mm. in diameter led into a vagina 4 cm. long (fig. 2). Uterus, tubes, and ovaries normal. No other abnormality of abdominal or thoracic viscera; no testes in abdomen or inguinal canal.

Microscopical examination of the kidney showed congestion, swelling, and cellular infiltration of the glomeruli, with degeneration of the epithelium of the convoluted tubules. Ovary, uterus, and vagina normal for age.



FIG. 2.—Horse-shoe kidney. Suprarenal enlargement (right suprarenal $4.5 \times 3.5 \times 1$ cm., weight 8.5 gm.; left suprarenal $3.5 \times 4 \times 1.2$ cm., weight 8.5 gm.) The small vaginal opening can be seen in the verumontanum, which lies at the lower end of the urethra.

The specimen shows the suprarenal glands, and the genito-urinary tract, with the exception of the terminal 5 mm. of the urethra.

Comment.—The relationship between suprarenal cortical hyperplasia and pseudo-hermaphroditism is well shown in this case. Development was probably normal until about the tenth week of intra-uterine life, but masculinization occurred after then. It is impossible to say whether in this case the hyperplasia bore any relation to the

development of horse-shoe kidney, but this abnormality is about four times as common in the male as in the female.

Sections of the suprarenals show that there was a large amount of medulla as well as of cortex. This may have caused the glycosuria and fatal renal failure, two features which have been noticed in similar cases, with simple hyperplasia or phaeochrome tumours.

Dr. PARKES WEBER said it was well known that hyperplasia—with or without actual tumour formation—of the suprarenal cortex in young females gave rise to the development of external masculine features, but that if the hormonal action in question had begun already, during intra-uterine life, the girl might be born with some degree of actual pseudo-hermaphroditism, that is to say, with congenital genito-urinary abnormalities of an externally masculine type, as in the present case.

Congenital Recto-sigmoid Stricture. — WILFRID SHELDON, M.D., and HAROLD EDWARDS, M.S.

Boy, aged 4 years.

9.6.33: Admitted when four weeks old. Constipated since birth, with occasional vomiting. First child. Normal labour. Abdomen distended.

On examination per rectum, narrowing of the bowel was found at the recto-sigmoid juncture. Sigmoidoscopy showed this to be a stricture admitting a No. 1 bougie. Dilated to No. 6 bougie; subsequently dilated on two occasions. On discharge, bowels were acting daily, and child was gaining weight.

26.8.33: Readmitted, aged 3 months. Had lost weight. Abdomen hard and distended. Colon loaded. Rectum empty. Stricture not patent to finger. Dilated several times and colon repeatedly washed out. Little improvement.

15.9.33: Stricture drawn down to level of anus and a wedge excised. Section showed plain muscle tissue with fair amount of fibrosis separating muscle bundles.

21.9.33: Complete obstruction appeared imminent. Left inguinal colostomy performed. Immediate improvement in the condition followed, and within four months the child's weight was doubled.

26.1.34: Attempted excision of stricture; unsuccessful, owing to high level. The emptying of the colon by the colostomy had allowed the stricture to recede. Silk thread passed through the stricture and a weight extension of 2 oz. applied in an attempt to draw the stricture down to a lower level, so that excision could be attempted.

2.2.34: Extension removed. Excision of stricture still not feasible. Colostomy belt fitted and patient sent home, still gaining weight.

8.2.35: Readmitted for investigation. Colostomy tended to prolapse. Catheter passed down easily through lower colostomy opening into rectum. Per rectum: stricture not so narrow as previously; admitted first finger.

4.4.35: Colostomy closed. Bowels acted normally with liquid paraffin but a month later signs of obstruction recurred. Colostomy wound reopened.

For two years no treatment was attempted and the child developed normally, the colostomy giving rise to little trouble.

Present day.—Rectum now seems almost normal. Digital examination: Remains of constricting band on anterior wall of rectum only. Large soft tube passes easily from lower colostomy opening through to anus, showing patency of bowel.

It is intended to make a further attempt to close the colostomy.

Comment.—The situation of the stricture appears to be unusual. It is of partly spasmodic type as shown by its response, after a few days, to dilatation and its steady improvement, almost to the point of disappearance, since the colostomy was made. The microscopical report, showing it to be mainly of muscle, confirms this.

Unusual Deformity of the Genitalia.—J. G. O'DONOGHUE, M.B., B.S. (introduced by Mr. HAROLD EDWARDS).

John C., aged 3 years 6 months.

Family history.—Apparently normal. No evidence of abnormality of any kind in the mother or father.

Apart from nocturnal enuresis there has been no complaint of any dysuria. Examination of the external genitalia reveals that (a) both testicles are normally present in the scrotum, which shows no abnormality. (b) The penis, as such, is represented by a loose fold of skin situated on the posterior portion of the perineal raphe and overhangs the opening of the anal canal. (c) There is a small external urethral opening on this fold of skin.

In every other respect the child seems healthy and is without abnormal signs.

Two Cases of Pyloric Stenosis treated with Eumydrine.—R. H. DOBBS, M.R.C.P. (by permission of WILFRED PEARSON, F.R.C.P., M.D.).

(I) Female child. Admitted on 18.2.37, when three weeks old, on account of vomiting.

Premature; weight 6 lb. at birth. Fed with ostermilk for ten days and then with lactogen. At one week vomiting began, and after ten days very little food was kept down. The bowels became constipated, two motions being passed during the week before admission.

Condition on admission.—Markedly dehydrated, and very thin; weight 5 lb. 1 oz. Visible peristalsis, a greatly dilated stomach, and a palpable tumour, about an inch to the right of the mid-line at the level of the pylorus.

Medical treatment was begun immediately, consisting of subcutaneous salines, a daily stomach wash-out for the first week and on every other day for the subsequent weeks. Child fed on frillac, 1½ oz. two-hourly. On this treatment the general condition improved although vomiting continued. The vomits were very large and occurred 2-4 times a day. The bowels acted on alternate days.

On the fifth day after admission X-rays showed barium to be entirely retained in the stomach up to six hours. The following day treatment with eumydrine commenced. For the first two days 25 minims of a 1:10,000 solution were given twenty minutes before each feed; subsequently the dose was reduced to 15 minims. There were five large vomits on the day before and on the day eumydrine was started; on the following day there was one, on the next two days there were two, and on the fourth day there was one small vomit. Thereafter, vomiting ceased. The bowels became loose, up to five and six stools being passed daily, and this, together with a slight pyrexia, lasted for ten days, after which the temperature settled and the stools became normal. The weight remained stationary for ten days and then increased on an average 2 oz. a day until discharge.

On the twenty-third day after admission eumydrine was discontinued for four days. The vomiting returned on the second day and ceased the day after eumydrine was resumed. On the twenty-eighth day X-rays showed that although there was still some retention of barium, considerable quantities had passed into the small intestines in four and a half hours. On the thirty-fourth day the child was discharged, weighing 7 lb. 3 oz. Peristalsis was still clearly visible but the stomach was appreciably smaller. The patient was subsequently treated by the home doctor.

(II) A five-weeks' old male infant admitted on account of loss of weight, vomiting, and constipation.

Second child. Birth-weight 7 lb. 5 oz. Breast fed entirely for two weeks, then partially until admission. Food started "pumping up" at two weeks, the stools became small but rather loose, and the child began to lose weight.

Condition on admission.—Moderately dehydrated, but general condition good. Visible peristalsis and palpable pyloric tumour. The bowels remained closed until the fourth day after admission. Medical treatment with subcutaneous salines and a daily stomach washout was begun on the day of admission. Feeding was with 2 oz. breast milk six-hourly, alternating with 2 oz. of frailac.

On the day after admission eumydrine was administered, $2\frac{1}{2}$ c.c. of a 1:10,000 solution being given half an hour before every feed. Vomits, which had occurred before almost every feed, were reduced immediately to one or two a day, and a week later to alternate days. The bowels became open on the fourth day and remained so until discharge.

On the fourteenth day the child was sent home on account of an outbreak of gastro-enteritis in the ward and was seen bi-weekly in the out-patients' department, eumydrine being continued. He continued to progress, having only occasional vomits, until three weeks after discharge, when there was a recurrence of vomiting during which visible peristalsis again occurred. It was found that the child had been receiving eumydrine made up more than ten days previously. A fresh stock was given, and vomiting disappeared in four days. At the end of ten weeks after admission eumydrine was reduced to $\frac{1}{2}$ c.c. before each feed, and the next week to the same dose before alternate feeds. On the thirteenth week after admission eumydrine was discontinued. There was no return of vomiting and the child continued to gain weight.

Comment.—These two cases illustrate a few important features in the treatment of pyloric stenosis with eumydrine. In Case I the child was severely dehydrated on admission, and treatment was delayed until sufficient fluid in the form of salines had been administered in order to replace both fluid loss and lost chlorides. In this respect pre-medication remains identical with that which should be carried out if operation is going to be performed. Efficient replacement of both water and chlorides, as indicated by a satisfactory diuresis, is essential before eumydrine is used if toxic symptoms are to be avoided.

In the same case, after twenty-three days, the drug was discontinued and vomiting returned until the drug was once again administered. On the other hand, in Case II eumydrine was given for ten weeks, and in Case I for twelve weeks after which it was gradually reduced in daily dosage until, at twelve and fourteen weeks, respectively, it was altogether discontinued, without any return of the vomiting. This is in keeping with what has long been taught in clinical medicine; that if the patient in a case of pyloric stenosis can, by any medical means, be kept alive for ten to twelve weeks an apparent spontaneous cure will result.

In Case II vomiting recurred when the drug, made up in a 1:10,000 solution, was kept longer than ten days. The eumydrine used for these two cases was dispensed from a $\frac{1}{2}\%$ stock solution mostly used for midriatic purposes, itself only replenished as required. It appears, therefore, that in very dilute solutions the drug "goes off", probably by hydrolysis, whereas in a stronger solution this action is insignificant.

Lastly, in both these cases the infants were discharged before treatment was terminated. In Case II, indeed, the child went home fourteen days after admission despite occasional vomits, and a return of the vomiting was satisfactorily dealt with in the out-patient department. If eumydrine, or any other form of therapy is to replace operation in the treatment of this condition, it is essential that hospitalization shall be as brief as possible. It is occasionally possible to discharge an operated case after seven days, though two or three weeks is a more usual time. There seems to be no reason why in favourable cases, diagnosed early, the patients could not be sent home within a week, though it remains to be seen whether eumydrine can be used in the out-patient department from the time the diagnosis is made.

Mediastinal Ganglio-Neuroblastoma.—F. DUDLEY HART, M.B. (introduced by Dr. B. SCHLESINGER).

Laurence B., aged 6. Admitted to hospital 25.1.37 complaining of pain in the abdomen intermittently for one week, pain in both knees and the left side of the face for one week, and small glands in the neck, painless and discrete, for four weeks. Previously he had been unwell for about a month. No definite tonsillar infection had been noted. The pain in the knees was not acute, but was made worse by movement. He had failed to gain weight for four months before admission. There was no history of cough, fever, or acute systemic upset. He had slept well, remained fairly cheerful, and had had a normal appetite until one week prior to admission.

Previous illnesses.—Measles and chicken-pox more than a year previously.

Family history.—Nothing relevant.

On admission.—Temperature 102.7° F., pulse 124, respirations 26. A thin boy, somewhat flushed, but quite cheerful. Small, discrete glands, very slightly tender, on both sides of the neck. Left tonsillar gland enlarged. Small shotty painless glands in both axillae. Examination of cardiovascular and respiratory systems revealed nothing definitely abnormal. Abdomen: Slight tenderness in both iliac fossae, but no rigidity. Liver and spleen not palpable. Joints: Slight pain experienced on moving both knees, also in left hip. No apparent abnormality otherwise. Central nervous system normal; no rash.

Blood: W.B.C. 8,000 per c.mm., polys. 54%, lymphos. 40%, monos. 6%. No abnormal red or white cells seen.

Mantoux reaction: Negative, 1:10,000, 1:1,000, and 1:100.

Progress.—The temperature came down to normal in four days, but occasionally rose to 99 or 100° F. Pulse and respiration also fell correspondingly.

16.2.37: Temperature 100.4° F. Pains in the neck. Glands much as before, but slightly more tender. Throat normal. Blood: W.B.C. 6,000 per c.mm., polys. 60%, lymphos. 32%, monos. 7%, basos. 1%. 4 myelocytes and 2 normoblasts per W.B.C. Sedimentation rate 53 mm. in one hour (micro method). The urine presented no abnormalities. The temperature had settled by 22.2.37, when a skiagram showed an oval mass behind the heart, alongside the vertebral column in the posterior mediastinum.

25.2.37: Blood picture as before. General condition improved.

6.3.37: Temperature 100.2° F., pulse 150. Very restless, with acute pain in the left knee. Movements free and painless at the knee, but much pain experienced on attempting to move the left hip, where the muscles were in spasm. Adduction, abduction, and flexion all equally painful. Nothing abnormal noted in the spine. Spleen not palpable. Left leg put in extension. Child rapidly improved, but an intermittent pyrexia persisted.

Later, 12.3.37, he had acute pain in the other hip with similar findings.

Operation (18.3.37) by Mr. Saner, under general anaesthesia. Left side of chest explored with a needle. No fluid found, but some resistance offered to the needle. A portion of the 9th rib was removed and an encapsulated tumour removed without difficulty from the posterior mediastinum. It was extrapleural, with no adhesions, except a few loose connexions to the surrounding structures. It was lying alongside the vertebral bodies opposite thoracic vertebrae 7th to 11th. There were no definite connexions at its lower pole.

23.3.37: Recovering from operation. Pale. Blood: Hb. 45%; R.B.C. 2,600,000; C.I. 0.9; reticulocytes 3%; W.B.C. 7,000 per c.mm.; polys. 60%; lymphos. 29%; monos. 6%; eosinos. 4%; basos. 1%. 4 megaloblasts; 1 normoblast; 3 myelocytes; and ? one myeloblast per 200 W.B.C. Many hypochromic R.B.C. Some anisocytosis and polychromasia.

Pathological report on tumour.—The tumour was encapsulated, with a firm yellow-white "cortex" and a red vascular "medulla", which in places came near the surface. Irregular in shape; $2\frac{1}{2}$ in. long, $1\frac{3}{4}$ in. wide, $1\frac{1}{2}$ in. thick.

Microscopically: "The solid tissue consists of a fibrillar matrix containing a number of pale rounded cells of varying size. These cells resemble sympathetic nerve ganglion cells. The hæmorrhagic tissue contains deeply staining rounded cells in masses, with some irregular rosette formation. There is much hæmorrhage and some necrosis. Diagnosis: Neuroblastoma, arising in a ganglioneuroma" (Dr. Ellison).

3.5.37: Still anæmic, but cheerful and free from pain; has latterly been allowed up, and walks well. Occasionally has slight pain in left knee as before. Hb. 65% on 23.4.37; is now 55%. R.B.C. had risen as high as 4,000,000 per c.mm. but have now dropped to 3,300,000 per c.mm. Colour-index has varied from 1 to 0.7. Immature red and white cells persist. X-rays have shown nothing abnormal in the hips or spine. It was thought that the spleen could be felt, following the transfusion,

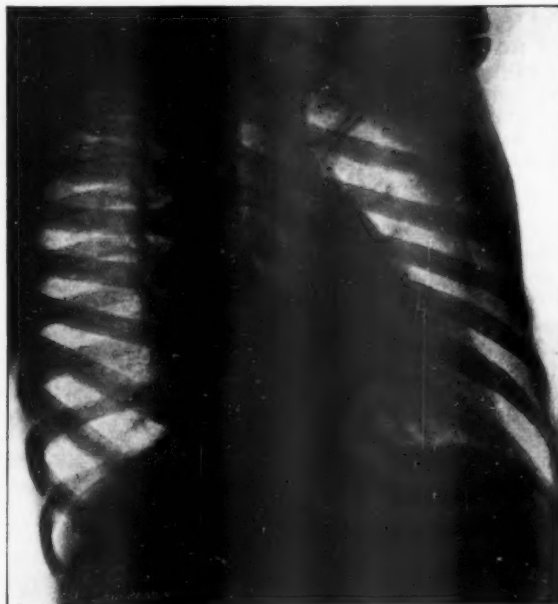


FIG. 1.—Right oblique view of the tumour mass.

but at no other time. Glands on right side of neck are definitely larger now. Central nervous system seems normal.

A histamine test-meal reveals no abnormality. Temperature occasionally rises and falls over an eight to eighteen day period, and is normal between, with occasional rise in the evening to 99.99.7° F.

Treatment.—The patient has had one blood transfusion, and is taking a liver extract and iron.

Comment.—The diagnosis was at first uncertain. A straight skiagram of the chest revealed nothing, as the shadow was hidden behind the heart, but on screening, the tumour mass was clearly seen in the right oblique position, and skiagrams in the lateral and right oblique positions showed it up well (fig. 1). A hard antero-posterior film (fig. 2) revealed its true extent.

The nature of the tumour is of interest. The outer cortex is firm and of a light yellow colour, containing large ganglion cells and generally presenting the appearance of a ganglioneuroma. The medulla resembles bone-marrow macroscopically—a red, semi-soft tissue. At the lower pole, where the cortex is narrower, it approaches the outer edge of the tumour. Microscopically this part is a neuroblastoma, and shows all cell types from the small undifferentiated formative cells (sympathogonia, as described by F. H. Wright), to immature ganglion cells (sympathoblasts). There was a rough attempt at rosette and ball formation here and there. The best description of such a tumour seems to be ganglioneuroblastoma, as suggested by H. E. Robertson. Necrotic and hæmorrhagic patches were also seen. Clinically

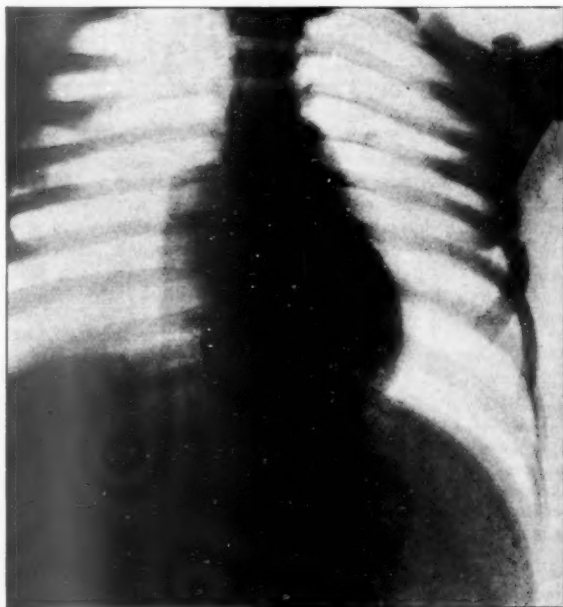


FIG. 2.—Showing the tumour mass behind the heart.

entral

rises
sional

liver

chest
g, the
n the
ntero-

and histologically such a tumour is half-way between the highly malignant neuroblastoma and the benign ganglioneuroma. Probably many of the tumours described under these two headings resemble the one described here. A true ganglioneuroma is said to be a rare tumour.

That the tumour in this case is malignant is shown by an increase in the size and number of cervical glands and a vaguely palpable mass in the left hypochondrium. The liver and spleen are now both enlarged. The anaemia persists as before and is taken to be a leuco-erythroblastic anaemia due to involvement of bone-marrow by the malignant process. Skiagrams of all bones have revealed nothing abnormal.

While in the ward the boy's condition has been good, but his temperature chart has shown two types of abnormality:—

- (1) A rise and fall, over a 5-to-12 day period, almost of a Pel-Ebstein type, and
- (2) occasional "spikes" of temperature lasting only 4 to 24 hours (fig. 3). Following such rises new glandular enlargements have been noted.

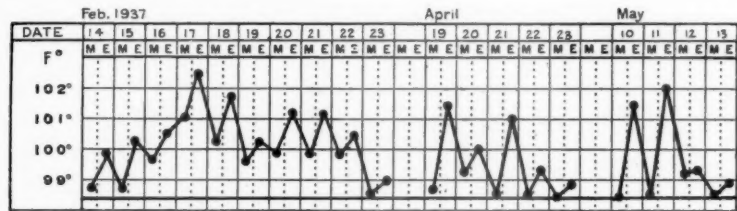


FIG. 3.—Showing the two types of abnormality seen in the temperature chart.

The acute pains in the hips are of interest, for they were noted in the early cases of adrenal neuroblastoma described. It is possible that they are in this case due to irritation of the spinal cord in the region of the tumour. Such cases have been described. Skiagrams of the hips show no bony abnormality.

The prognosis is bad, but the downward path is very slow, and at present the child is living a happy life, and is up and about the ward.

Discussion.—Dr. F. PARKES WEBER asked what the histological appearance of the enlarged lymphatic glands was likely to be. He supposed that they would not contain (metastatic) ganglion cells.

That the blood-counts showed slight erythroblastosis was not surprising in the case of a child whose bone-marrow probably reacted more easily than that of an adult towards neoplastic metastases. In adults, however, a very high degree of erythroblastosis had been found in some cases of generalized miliary (or rather submiliary) metastatic dissemination in the bones, from primary prostatic carcinoma.

Dr. G. H. NEWNS said that, by the courtesy of Dr. Schlesinger, he had seen this case some weeks previously. He was interested in it because he was engaged, in collaboration with Dr. Ruby Stern, in a study of neuroblastoma in children.

There were three points of interest. First, the histological appearance of the tumour was unusual. The outer solid part was a typical ganglioneuroma, many adult ganglion cells being present. The central hæmorrhagic part was quite different. The cells were sarcoma-like in appearance, very primitive, and actively growing; several pseudo-rosettes were to be seen. This tumour in his view had been at first a ganglioneuroma; later the central part had become malignant and "thrown back" to the tumour derived from the more primitive cells of the sympathetic series.

Secondly, the Pel-Ebstein type of curve was striking. Analysis of his series showed that a periodic temperature was common: in one case the curve resembled the Pel-Ebstein type.

Thirdly, the blood picture was most interesting. While in one or two cases of his series there were nucleated red cells in the peripheral blood, nothing resembling the leuco-erythroblastosis in this case had been seen.

The explanation was, he thought, the presence of a diffuse cellular infiltration of the bone-marrow, producing pressure on the hæmopoietic cells. An intense hyperplastic response resulted, and primitive cells appeared in great numbers in the peripheral blood. No radiological changes would occur, such as would be seen with massive bony deposits.

Section of Medicine

President—Sir CHARLTON BRISCOE, Bart, M.D.

[May 25, 1937]

Three Cases of Eunuchoidism

By A. C. CROOKE, M.D.

A DESCRIPTION of the condition of eunuchoidism is sufficiently rare in the English literature to warrant a report on the following three cases. Capel (1935) published the description of a case in a male, similar to my first case, and Zondek (1935) illustrated in his book cases similar to my first and third cases. My second case is of especial interest in that it occurred in a female and has many features in common with the case reported by Aitken (1933). In this last case an atypical teratoma and spheroidal-celled carcinoma of one ovary had been removed eleven years previously and it was considered that this operation had some direct bearing on the eunuchoidism. The patient, now aged 27, is still attending the London Hospital and has grown considerably since Aitken's report was published.

Case I (fig. 1).—F. A., a man aged 30, was born of English parents in India where he has lived practically all his life. He was sent to England to see Mr. Hugh Cairns, as possibly having a pituitary tumour, on account of his eunuchoid condition and fits, and was admitted to the medical unit of the London Hospital in February, 1936. He had lived an active, out-of-doors life among natives. On rare occasions when he met other white men he was accustomed to take large quantities of alcohol, up to a bottle of whisky in an evening. Nine months before admission, he obtained a sedentary appointment, and constantly associated with other white men; consequently he had frequent bouts of excessive drinking. He asserted that no amount of alcohol made him drunk. Two and a half months before admission and the day following one of these bouts he had the first fainting attack. He had a sudden sinking feeling, everything went black in front of his eyes, and he had buzzing in the ears. He did not lose consciousness. Subsequently he had many similar attacks. He had been much worried about his physical condition, always preferring to associate with men and to avoid women. He developed normally during childhood but growth had continued at rather a rapid rate during adolescence and at the age of 23 he was 6 ft. 1 in. high. Since then he has grown another inch and thinks he may still be growing slowly. He takes the same size in hats and boots as he did at the age of 21. He has weighed as much as 15½ stones but has lost 16 lb. recently by dieting. His external genitalia and secondary sexual characteristics never developed normally during adolescence. He has had penile erections since adolescence but no orgasm. He has never been able to have, nor has he desired, sexual intercourse. He grows a fine down on his chin which he shaves twice a week. His voice has never broken but he has cultivated a deep tone to simulate that of an adult man.

At the age of 19 he had a course of injections of "testogen" in London without any noticeable effect.

Previous history.—Smallpox, measles, mumps, and malaria.

Family history.—Father died of Bright's disease. Mother died of sprue. One brother died of angina pectoris, aged 52. One brother, 6ft. in height, one

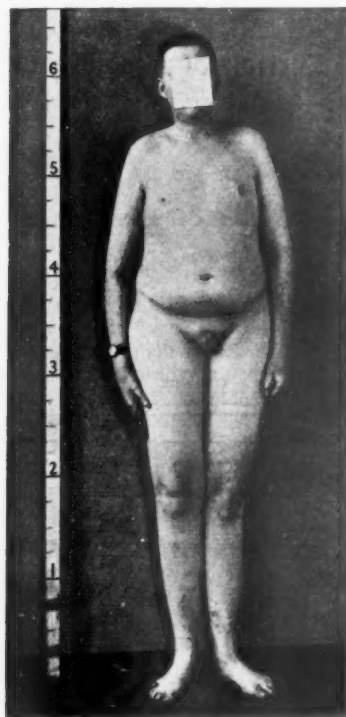


FIG. 1.

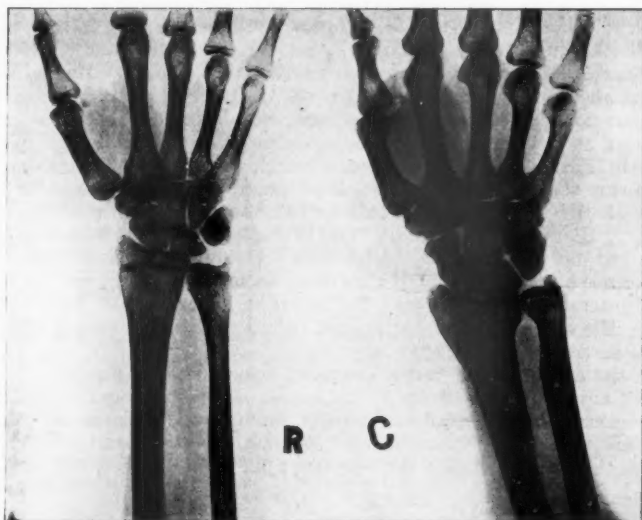


FIG. 2.—Forearm (Case I) R, with that of normal male control C, aged 27; height 6 ft 2½ in.

5 ft. 9 in., and two sisters, both 5 ft. 6 in., are all alive and well. Two died in childhood. No other members of his family are similarly affected.

On examination.—Big, tall, sallow-complexioned man with sunken eyes and unusually prominent maxillary prominences. No prognathism. Teeth crowded with an extra right upper lateral incisor. Eyebrows slight. Eyelashes scanty, especially the lower ones. Moustache and beard completely lacking. Complete absence of hair on the body and only fine down on the extremities; axillary hair absent; a few scanty pubic hairs only. Narrow shoulders; exceptionally broad hips. Some lower abdominal—but no gluteal—adiposity. No suggestion of breast development, the nipples being smaller than those of the average male. Supernumary nipple present on both sides. Tiny penis (1 in. long) and scrotum containing very small soft testicles and epididymes normal in size for a boy before the age of puberty. Heart normal. Blood-pressure 130/80. No abnormal physical signs in the central nervous system, lungs, or abdomen.

Skiagrams of epiphyses (fig. 2) showed union incomplete in phalanges and metacarpals; lower radial and ulnar not united; upper radial and ulnar united; lower humeral united; upper humeral not united; lower tibial and fibular, upper tibial and lower femoral incompletely united; upper femoral united; iliac crests incompletely united. Compared with the normal control there appeared to be considerable osteoporosis. A direct sellar skiagram suggested some diminution in the vertical diameter of the fossa.

Blood-count showed slight secondary anæmia. Sugar tolerance, renal efficiency, plasma chlorides and basal metabolic rate normal. Fluid intake and output normal.

Case II (fig. 3).—R. L., a Polish Jewess, aged 41, admitted to the medical unit of the London Hospital in March 1936 from the massage department, where she had been attending for treatment of her rheumatism of many years standing. She was complaining of great nervousness, restlessness, sweating and palpitations and frequent morning occipital headaches. She was continuously brooding over her malformation. She came to this country at the age of 17 and married at the age of 24, at which time she weighed 16½ stones. She was always tall for her age and does not know when she stopped growing but does not think she has grown since the age of 21. As a girl she used to get attacks of lower abdominal pain lasting for two days; these disappeared when she married. Her periods have never commenced and about 10–15 years ago she had a vaginal examination for sterility and was told she was infantile. Her breasts are still infantile.

Previous history.—Nervous breakdown in 1922. Abscess in left ear five years ago.

Family history.—Father died of pneumonia. Mother alive and well. Three brothers and two sisters alive and well, all shorter than herself.

On examination.—Very big woman, 5 ft. 10 in. high, but stature diminished by marked kyphosis and marked genu valgum (2½ in. between internal malleoli). High coloration; rather high cheek bones. Hair of head abundant and of very fine texture; used to reach down to buttocks. Slight excess of hair on upper lip. Eyebrows scanty; eyelashes short and somewhat scanty. Scanty pubic hair; absolutely no down on trunk or extremities. Purplish discoloration of hands; fingers long, tips tapering, little finger definitely short (½ in. short of crease between distal and middle phalanx of ring finger). Purplish-plum coloration of legs. Breasts poorly developed; nipples small. Heart normal. Blood-pressure 140/90. No abnormal physical signs in central nervous system, lungs, or abdomen. A pelvic examination was made by Mr. Brews under a general anæsthetic. He reported a large mass of fat in the position of the mons veneris. Labia majora and minora underdeveloped. Clitoris relatively well developed

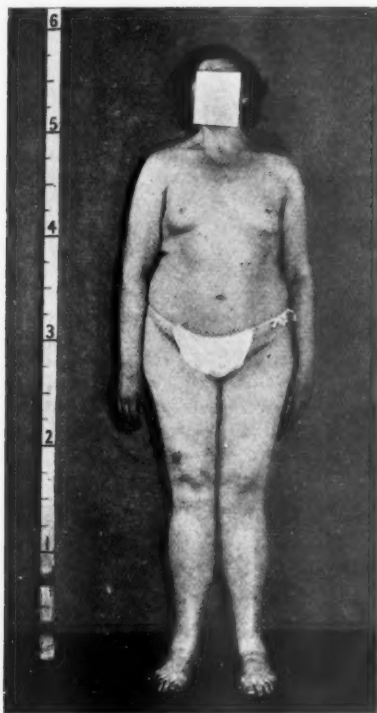


FIG. 3.



FIG. 4.—Skiagram of uterus (after injection of lipiodol).

Vaginal orifice normal in size. Vagina seemed normal in length and circumference; underdeveloped vaginal cervix. Slight cystocœle. Body of uterus not felt; ovaries not felt. Promontory not felt at $4\frac{1}{2}$ in. Uterine sound passed easily upwards and forwards $2\frac{1}{2}$ in. Lipiodol was injected and an X-ray examination showed an unusually small uterus and patent tubes (fig. 4).

A skiagram of the epiphyses shows the line at which union had taken place in all bones in the hand; well shown at the proximal ends of the phalanges and the lower end of the radius; normal union in the upper end of the radius, and the ulnar and lower end of the humerus, and a slight suggestion of a line of union in the upper end of the humerus; the line is well shown in the lower ends of the tibia and fibula; a double line is shown in the inner side of the upper end of the tibia; a line is well shown in the lower end of the femur; union is complete in the upper end of the femur; not quite complete in the iliac crests.

Case III (fig. 5).—S. A., an unemployed seaman aged 47, was first admitted to the London Hospital, under Dr. Parkinson, in December 1934 on account

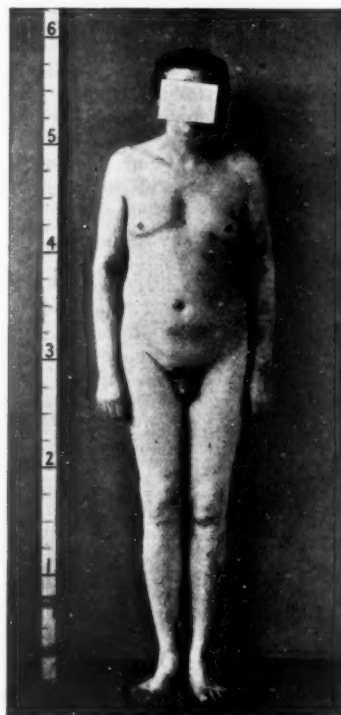


FIG. 5.

of his cardiac condition. He gave a history at this time of breathlessness on exertion but also while at rest, the attacks lasting up to half an hour at a time. He was found to have aortic stenosis and incompetence.

Readmitted on the Medical Unit in April 1937 for investigation of his eunuchoidism. He had not complained of any symptoms in connexion with this and the following history was only obtained with some difficulty. He has been at sea most of his life and travelled all over the world. His shipmates have always teased him about the size of his breasts and told him that he was really a woman. He used to have a voice like a woman until only about three years ago. It has gradually become deeper of late. He has never liked women. Never had, nor desired, sexual intercourse; has never had penile erections or orgasm.

Previous history.—Chorea as a child. No history of mumps. Appendicectomy 10–12 years ago, in Panama. Emergency operation for ? perforated gastric ulcer in South America six years ago.

Family history.—Father died of enteric fever. Mother died of cancer. Six brothers and sister all married and have children.

On examination.—Rather childish mentally but co-operative. Strong, heavily built man, height 5 ft. 10½ in. Extensively tattooed. Tone of voice unusual; not that of an adult male nor that of a child, but probably cultivated from an unbroken voice. Skin sallow and unusually soft and fine. Hair on scalp plentiful, straight, long, and fine. Complete absence of hair on face, trunk, arms, and legs. Scanty pubic hair, of female distribution. Breast tissue probably not increased, but surrounded by an excessive amount of fat, giving a pendulous appearance. Excess of subcutaneous fat. Penis normal but rather small; very small testicles, approximately ¾ in. × ⅝ in. Heart slightly enlarged to left. Loud rough systolic murmur and thrill over whole precordium, loudest in aortic area; soft diastolic aortic murmur. Blood-pressure 110/60. No abnormal physical signs in central nervous system, lungs or abdomen. Skiagrams of all long bones showed normal union of epiphyses with diaphyses. Pituitary fossa normal.

The first two cases are evidently clinically similar, and one of the most outstanding features is the marked delay in closure of the epiphyses, with consequent continuance of growth beyond the normal time. It seems reasonable to suggest that the genitalia have never developed because of a deficiency of pituitary secretion, presumably the gonadotropic hormone. Evidence is accumulating that the gonadotropic hormone exerts some influence on the closure of epiphyses. Typically there is marked delay of epiphyseal union in the pituitary dwarfs. When these cases are treated with growth hormone there is a great spurt in the rate of growth which tends shortly to become arrested, owing to union of the epiphyses. It is thought that this is due to contamination of growth hormone with gonadotropic hormone; for the former has not yet been adequately purified.

It seems probable that the third case is a separate clinical entity, and not one of eunuchoidism developing at a later period of life than in the first two cases. If it was due to the latter condition, one would have expected the epiphyseal union to have been delayed in this case also.

I am indebted to Professor Arthur Ellis for permission to publish these cases and to the X-ray department of the London Hospital for the X-ray plates and reports.

REFERENCES

- AITKEN, R. S. (1933), *Lancet* (ii), 1252.
CAPEL, E. H. (1935) *Lancet* (ii), 886.
ZONDEK, H. (1935), "Diseases of the Endocrine Glands", London.

Dr. F. PARKES WEBER said that it was interesting to compare this class of tall hypogonadic subjects with Hastings Gilford's class of ateleiotic dwarfs. In both classes there was "ateleiosis" (unfinishedness) of the epiphyseal development and of the sexual organs, but, whereas in primary hypogonadism there was no ateleiosis in regard to length of the body, in Gilford's cases there was definite dwarfism. It would be of great help if the pituitary glands in the two classes could be carefully examined by modern histological methods, especially in regard to their eosinophilic cellular constituents.

The Differential Diagnosis of Mediastinal Tumours

By N. LLOYD RUSBY, M.R.C.P.

MEDIASTINAL tumours, in general, may be either benign or malignant, cystic or solid. Their histological structure ranges from the simplest type of benign tumour, such as the lipoma, to the extremely complex teratoma, the architecture, of which displays such a high degree of organization that it well merits the description of a foetal parasite.

In the time available, it is impossible to discuss separately and in detail each type of tumour that has its origin in the mediastinum; moreover, it would be of doubtful value to do so, as in many instances the final diagnosis is only attained by a microscopic study of the tumour after operation has been performed or after the death of the patient. I propose, therefore, to indicate first the lines along which such a case might be investigated in order to establish during life and before operation the probable pathology of the condition, and then to refer to a few individual tumours which have certain characteristics of their own whereby they may be recognized by the clinician.

The history of the patient is important in distinguishing a tumour of the mediastinum from other diseases which may simulate it. For example, a history of specific disease, many years before, may engender a greater caution in diagnosing tumour rather than aneurysm of the aorta; the history of an intimate contact with a phthisical parent in the case of a seedy-looking child may incline the physician to diagnose tuberculous mediastinal lymphadenitis as the cause of the dry, hacking cough rather than Hodgkin's disease or lymphosarcoma of the thymus.

Benign tumours of the mediastinum may cause no symptoms whatsoever. At the end of last century, before the advent of X-rays, they were commonly found during the performance of a routine autopsy, while to-day their presence is sometimes disclosed in the X-ray plate taken to exclude phthisis in a tuberculous contact. When symptoms do become manifest they are the result of either the pressure of the tumour within the thorax or the supervention of some complication, such as hæmorrhage, infection, or of a bronchial fistula. The dermoid cyst is the only tumour of the mediastinum that can boast a pathognomonic symptom. The Chinese woman, quoted by Eloesser (1933), would not have spent two years in a sanatorium for repeated hæmoptyses, due to a presumed small tuberculous focus at the hilum, if more attention had been paid to the husband's observation that she occasionally spat up hairs in her sputum. It is only rarely, however, that dermoid cysts disclose their identity in this way.

The physical examination of the patient may or may not reveal the presence of disease. If abnormal physical signs are found in the chest, they are open to misinterpretation in the absence of radiological support. The literature contains numerous instances of mediastinal cysts being mistaken for pleural effusions, encysted empyemata, cases of bronchiectasis, phthisis, and other conditions. The first case of dermoid cyst of the mediastinum ever reported, that of Gordon's (1823), was thought by him, first of all, to be pneumonia and later, when it presented in the neck, an aneurysm of the innominate artery.

When once infection in a cyst has occurred, the resemblance to an empyema is very striking: the toxic appearance with high fever and clubbing of the fingers associated with signs of fluid in the chest has often led the physician to invite surgical aid. Even rib resection and drainage, however, do not necessarily reveal the true nature of the condition.

It is often impossible, before metastases are evident and cachexia is apparent, to distinguish between a benign and a malignant tumour of the mediastinum, although

to do so early in the disease would be in the best interests of the patient. I think, therefore, that it would be worth while to mention two points which Harrington (1930) in America has found of value in forming an opinion.

The first is pain. It is remarkable to what size a benign tumour of the mediastinum can attain without causing any pain at all. On the other hand, a smaller tumour may be associated with very severe pain indeed. It is this excruciating pain which often becomes worse when the patient is in bed at night and which is the result of a relatively small tumour that suggests malignancy.

The second point is the recognition of Horner's syndrome. Harrington believes that Horner's syndrome occurs more frequently in malignant than in benign cases and attributes this to actual infiltration of the cells of the inferior cervical ganglion by malignant growth rather than to the simple pressure on the ganglion of a benign tumour.

There is no doubt that in the differential diagnosis of mediastinal tumours a detailed radiological investigation is of the greatest service. It is clear that the simple antero-posterior view of the chest is, as a rule, inadequate in itself and tells little more than which side of the chest is affected. When it is combined with a straight lateral, valuable information is obtained as to the shape of the tumour; its probable size; whether its edge is clear-cut or ill-defined, homogeneous or nodular, and—what is very important—whether the tumour lies in the anterior or posterior compartment of the mediastinum. Films taken in the oblique plane often furnish a better idea as to the structures to which the tumour is adherent; whether, for instance, it is attached to, or is distinct from, the aorta. A stereoscopic view of the chest is also an asset.

The fluoroscopic screening of the patient is almost as important as a study of the X-ray plates, and supplies data of a peculiar character. On the screen any pulsation of the tumour can be demonstrated and its relation to the aortic shadow can be made out in even greater detail, particularly if a barium swallow is used. The diagnosis of an intrathoracic goitre can be made with fair assurance from the screening alone, for not only does it present itself as a wedge-shaped tumour with the apex of the wedge directed downwards, but it can often be seen to elevate on swallowing.

The possibilities of radiological examination are not yet exhausted. It can be combined with certain other procedures to elicit facts of the greatest value. The first of these is the induction of an artificial pneumothorax in the absence of gross pleuritic adhesions. An X-ray picture will now show the relationship of the mass to the pleural space and whether it lies within or outside of the lung substance. Furthermore, if the tumour is cystic and the distinction between it and a pleural effusion a difficult matter, it is possible to introduce air through a needle into the cyst and a skiagram taken erect will show a fluid level within the cyst. This appearance in conjunction with an artificial pneumothorax is presumptive evidence of a cyst and it becomes even more striking if the picture is taken with the patient inverted. This technique was used recently by Skinner and Hobbs (1936) to demonstrate the cystic nature of a tumour, diagnosed clinically as a pleural effusion, and proved later, by microscopy, to be a cystic lymphangioma of the mediastinum.

Finally, contrast-radiography, with lipiodol, is an accessory measure which is often very useful. A complication, by no means rare, of a mediastinal tumour, is the gradual development of a secondary bronchiectasis. A comparatively small dermoid cyst, for example, lying on the right side of the mediastinum near the hilum of the lung can cause, by pressure on the middle lobe bronchus, a dilatation of the bronchi beyond the site of obstruction. Similarly, a larger tumour can produce the same sequence of events in the upper or lower lobes of the lung. It is frequently a difficult matter to decide whether certain symptoms, such as hæmoptysis or the expectoration of a thick purulent sputum, are due to the cyst or are the result of the bronchiectasis to which it has given rise. From the point of view of surgical treatment, it is obviously

important that this should be settled, since the complete removal of the tumour will effect a cure in the one case but in the other is unlikely to be of much benefit.

The presence of an infected bronchiectasis producing sputum can be inferred indirectly by the exploration of the cyst. Many of these cysts are so large and resemble an empyema so closely that they have been tapped before the correct diagnosis was realized. The fluid withdrawn can be compared with the expectoration of the patient. If doubt still exists, a few cubic centimetres of methylene blue injected into the cyst will disclose the presence of a bronchial fistula by tinting the sputum in the matter of a few hours. A more acute and more satisfactory way of solving the problem, however, is with the aid of lipiodol. If bronchial dilatations are present and the oil is seen to enter the whole lung field, then these dilatations will be revealed; if, on the other hand, lipiodol can be demonstrated within the cyst, it is diagnostic of the presence of a bronchial fistula.

The bronchoscope is not of much value in diagnosis of these tumours. It will help to exclude a primary bronchial origin or, if the tumour is extra-bronchial, it may reveal constriction of the tube. The thoracoscope also is of little help. It may, however, assist by showing, with greater accuracy than X-rays, to which structures in the mediastinum the tumour is adherent.

If the nature of the tumour is still in doubt, an exploratory thoracotomy should be carried out in carefully selected cases. The operation should be planned so that, if necessary, the incision can be enlarged and the tumour removed. As a rule, the operation employed for diagnostic purposes is safe in skilled hands but there is an element of risk, particularly if a biopsy is performed.

To consider certain of these tumours in more detail: As a class they are rare. It appears from the literature that of those tumours that take origin primarily in the mediastinum the dermoid cysts and teratomata form the largest individual group—well over two hundred having already been put on record. There is no hard and fast line of distinction between a dermoid cyst and a teratoma; the former is usually regarded as being derived from one germinal layer only, whereas the latter contains elements of all three layers of the blastoderm. In point of fact, many specimens consist of both types of tumour, having the outward appearance of a dermoid and exhibiting perhaps, at one pole, a solid tumour which microscopy proves to be an undoubted teratoma. The comprehensive name of terato-dermoids has been suggested for the entire group, with the pure teratoma at one end of the scale and the apparently pure dermoid cyst at the other. The teratoma is the more malignant of the two and usually produces symptoms at a slightly earlier age.

Dermoid cysts of the mediastinum have been found in young children and in the aged, but the commonest age-period for the onset of symptoms is between 20 and 35 years. They occur characteristically in the anterior mediastinum and I have not found in the literature a case, the pathology of which was undisputed, in which the cyst arose from the posterior compartment. They may, of course, by their enlargement, encroach upon one or other side of the chest, or extend backwards towards the spine. They can be diagnosed with certainty if hair can be found in the sputum, and there are cases on record in which a drainage operation has been performed, in the belief that it was an empyema, and hair has been found in the discharge issuing from the chest. Examination of the sputum also affords further corroborative evidence if it is found to contain sebaceous material and cholesterolin crystals.

Radiologically there may be difficulty in distinguishing a dermoid cyst from an aneurysm of the aorta. They often look exactly alike. The edge of the dermoid cyst may be completely calcareous, or deposits of calcium be seen within it. If the tumour exhibits pulsation on the screen it is more likely to be an aneurysm, but aneurysms of the aorta do not always pulsate. The Wassermann reaction will help, but Paul White gives a figure of 15% negative Wassermann reactions in

cardiovascular syphilis taken as a whole, and it is always possible that in a case of dermoid cyst the patient may suffer from co-existing syphilitic disease.

There is another class of cyst, probably embryonic in origin, that is found usually in the posterior mediastinum. The histological structure of these cysts very closely resembles that of the normal stomach, the fetal oesophagus, or the bronchus, and occasionally both gastric and bronchial elements may occur together in the same specimen. Only a few cases have been reported, but they seem to occur in young children. They are sometimes very large, and occasion attacks of respiratory distress and cyanosis which are often severe a few moments after a meal. In this respect they resemble cases of diaphragmatic hernia in infants.

Tumours of mediastinal glandular origin occurring in children are often difficult to diagnose with certainty. The points of distinction between tuberculous lymphadenitis and Hodgkin's disease are outside the scope of this paper, but both diseases must be distinguished from a teratoma and a lymphosarcoma of the thymus. Many lymphosarcomata of the thymus are tri-lobed tumours and they are found in the anterior mediastinum.

In conclusion, I will just mention the mediastinal lipomata. They are very rare, only twenty-six cases having been reported in the literature. In quite a number of the cases they consist of an intrathoracic and an extrathoracic portion joined by a pedicle which pierces the thoracic cage—the so-called hour-glass or dumb-bell tumour. They may be symptomless or may cause discomfort through pressure. They may attain a very large size. In those cases which are entirely intrathoracic, their recognition is difficult but, as Walker (1936) has recently suggested, the exploring needle can give a clue. No matter what bore of needle is used and no matter to what depth it is inserted, no fluid will be obtained; furthermore, the sensation is that of exploring a pat of butter, and at no stage is there experienced a sense of resistance such as is encountered when the needle penetrates the wall of a dermoid cyst.

Such is a very brief—and, I fear, inadequate—résumé of some of the diagnostic difficulties of mediastinal tumours. Their accurate recognition and successful treatment demand the combined skill of the physician, the radiologist, the pathologist, the anaesthetist, and of the thoracic surgeon.

REFERENCES

- ELOESSER, LEO (1933), *J. Thoracic Surg.*, **3**, 71.
GORDON, J. A. (1927), *Medico Chirurgical Transactions*, **13**, 12.
HARRINGTON, S. W. (1930), *Surg. Gynec. and Obst.*, **51**, 647.
SKINNER, G. F. and HOBBS, M. E. (1936), *J. Thoracic Surg.*, **6**, 98.
WALKER, R. MILNES (1936), *J. Thoracic Surg.*, **6**, 89.

Chronic Miliary Tuberculosis

By J. M. VAIZEY, M.D.

THE term "miliary tuberculosis" has been used in clinical medicine for many years to describe an acute and fatal malady, and only in recent times, with the help of radiography, has it been possible to recognize chronic, arrested, and healed forms of this condition. There are now more than 130 convincing cases reported.

For the term "miliary tuberculosis" some definition is clearly desirable, and it is used here to describe a condition characterized by multiple discrete lesions approximating in size to a millet seed and due to the tubercle bacillus. Such lesions are not necessarily all hæmatogenous, and further hæmatogenous tuberculosis is often massive and not miliary, so that the use of miliary tuberculosis as synonymous with hæmatogenous tuberculosis is incorrect.

During life it is usually only possible to see the lesions in the lungs by radiography, though occasionally they may also be seen in the spleen and liver, so that in practice the diagnosis which can be made is usually only chronic miliary tuberculosis of the lungs.

The condition is most frequently found in children and young adults. The clinical features vary widely in such patients and the following provisional classification has been adopted in the analysis of 120 cases.

The first group consists of those patients with a course ending fatally in from three to six months (any case of less than three months' duration is regarded as an acute case). The patients in this group usually had an abrupt onset with pyrexia, dry cough, dyspnoea, and cyanosis, and pursued a febrile course without remissions. The cause of death was usually meningitis or tuberculous toxæmia. These cases thus closely resembled cases of acute miliary tuberculosis, and differed only in that their duration was abnormally great.

The second group consists of those patients who died after a course of more than six months. The average duration was about two years and the longest eight years. These, in contrast to the first group, often had a much more insidious onset, with general malaise but without much pyrexia. A further point of distinction from the first group was the presence of remissions, when the patient was afebrile and symptomless, and sometimes even managed to return to work. Such remissions were, however, always of short duration—nearly always less than a year—and the patient then relapsed, with symptoms of renewed spread. Another striking difference was the large number of patients who showed evidence of extrapulmonary tuberculosis clinically. This might be in the bones and joints, in the renal tract, in the eyes or in the skin. Often, clinically, these were the first lesions recognized and only on routine radiography was miliary tuberculosis of the lungs discovered. The cause of death varied greatly in this group, for though many died of a fresh tuberculous dissemination, with meningitis or toxæmia, some died of renal tuberculosis or suprarenal tuberculosis, while the pulmonary lesions remained quiescent. A few patients died of right heart failure, presumably due to stenosis of pulmonary vessels by pulmonary endarteritis.

The third group consists of those who recovered and remain alive and well. The criterion of recovery is taken as two years' complete freedom from all symptoms of tuberculosis, as experience has shown that relapse after this time is very infrequent. Some of these patients had a tuberculous lesion outside the lungs and the pulmonary lesions remained throughout clinically unimportant; others had some fever, cough, and malaise at the onset, but this was usually slight and transient. An uninterrupted recovery was the rule with such patients though a relapsing course was sometimes seen. A subgroup may here be mentioned in which the whole disease passed unrecognized, and was only later discovered accidentally, by radiography, or at necropsy, after death from some unrelated condition.

Physical signs.—There is nothing characteristic on examination of such patients. In the acute stages pyrexia, tachycardia, dyspnoea, cyanosis, and lassitude are seen and tuberculosis in the eyes, the bones, or the renal tract, may be found, but in the lungs there are usually no abnormal signs and they are never characteristic. The condition has therefore to be recognized by radiography.

Radiography.—The characteristic radiographic appearance is that of multiple small opacities covering both lungs and scattered uniformly throughout the field. In the more acute stages they are often soft and ill-defined, giving a hazy ground-glass appearance, but in the chronic forms the opacities are usually harder and more discrete with clear intervening lung tissue. Occasionally fine striæ are seen joining the miliary opacities, and these are probably due to a spreading lymphangitis.

The diagnosis has to be made from other conditions which may produce a similar radiographic picture. Of these the most important is probably pneumokoniosis,

and the history of exposure to harmful dust over a long period is the essential point in distinguishing this condition. Secondary carcinomatosis has also to be considered but this occurs usually later in life, is rapidly progressive, and the primary growth can generally be discovered. There are a great number of other conditions which may occasionally lead to confusion. Disseminated bronchopneumonia, congestive heart failure, and the miliary forms of syphilis, Hodgkin's disease, actinomycosis, aspergillosis, amyloidosis, and xanthomatosis are among these.

Positive proof that the opacities in the lungs are due to tuberculosis cannot always be obtained during life. Tubercle bacilli are found in the sputum in only about half the cases and in a few others are found by gastric lavage or analysis of the stools. Evidence of active tuberculosis in a further 20% may often be found elsewhere by biopsy or urine analysis, and then there is a very strong probability that the lesions in the lungs are also tuberculous. Even when such proof is lacking, miliary tuberculosis may still be the most likely diagnosis and such tentative diagnoses have been confirmed by necropsy in a few.

In conclusion, multiple small discrete opacities seen in a skiagram of the chest are quite likely to be miliary tubercles, but they do not necessarily indicate a hopeless prognosis. When they are found in association with tuberculosis elsewhere they do not therefore contra-indicate local treatment, even by operation if necessary, though they do probably make the ultimate outlook less hopeful. Their activity and importance must be assessed by the other clinical features of the case, especially the presence or absence of toxæmia.

REFERENCES

- BURNAND, R., and SAYÉ, L. (1924), *Ann. de méd.*, **15**, 365.
HAUTEFEUILLE, E. (1926), *Thèse de Paris*.
HEIN, J. (1930) *Beitr. z. Klin. d. Tuberk.*, **74**, 3.
HOYLE, C. and VAIZEY, M. (1937), "Chronic Miliary Tuberculosis", London.

Section of Surgery

SUB-SECTION OF PROCTOLOGY

President—G. GORDON-TAYLOR, O.B.E., M.S.

[May 19, 1937]

The Incidence and Treatment of Diseases of the Colon.¹

By Sir EDMUND SPRIGGS, K.C.V.O., M.D., F.R.C.P.

OF late years much has been said and written about the colon, and a good deal has been done to it. It has, on the one hand, been abused for its sins and, on the other, pitied for its sorrows. There are those who would stimulate and those who would soothe; those who would make fast, loosen, or denervate. And we have enjoyed some spirited writing, and seen much enterprise displayed, on one view or another, both by physicians and surgeons.

The state of the colon has a profound effect upon the well-being of the body. It shares with the gullet and the stomach, but not the small intestine, a proneness to disease, with a tolerance to investigation and treatment from without. Thus, it can be examined easily and, as a subject for discussion, has advantages; for there is less conjecture as to its state than is the case with diseases of many organs, and illustrations can be provided on the screen.

Among comprehensive writings of observers, I may mention those of Niklas, Lockhart-Mummery, Hurst, Lord Dawson, Manson-Bahr, and latterly Rankin, Bagen, and Buie.

INCIDENCE OF COLONIC DISEASE

In classifying into large groups the records in our clinic of over 8,000 cases, it appears that about one-third suffered from some vascular or cardiac disease, whilst one-half sought relief for some disorder of, or connected with, the alimentary canal and its accessory glands. Of these, 1,574 had an affection of the colon, with the distribution shown in Table I.

TABLE I.—DISEASES AND DISORDERS OF THE COLON

To October 1936		Per cent.
Diverticulosis (including prediverticular state 139, diverticulitis 120)	612	38.8
Colitis (including catarrhal or muco-membranous, spastic and entero-colitis [17 = 1.2%])	535	34.0
Dysentery	33	2.1
Post-dysenteric colitis	17	1.1
Other parasites	44	2.8
Ulcerative colitis and colitis gravis	51	3.2
Celiac disease and sprue	19	1.2
Growth (excluding rectum)	64	4.1
Tuberculosis (also with enteritis 2)	7	0.5
Polypus	14	0.9
Obstruction	28	1.8
Volvulus	8	0.5
Redundant sigmoid	142	9.0
	1,574	100.0
Simple delay, proved radiologically	1,507	
Dropping (of stomach also in 88)	304	

This list differs in important respects from the analysis of 1,564 cases of functional diseases of the colon, published in the *Quart. J. Med.* (1931, 24, 534). It is a coincidence that the total numbers of cases in the two records should be near together.

¹ Part of an opening address at the biennial conference of the New Zealand Branch of the British Medical Association held at Wellington on Tuesday, February 23, 1937.

It is seen that the commonest colonic disorders were the various forms of colitis, including dysentery, but in England diverticulosis, with its complications, is almost as common. In a number of cases of diverticulosis, however, the complaint is quiescent, being recognized at the X-ray examination of a patient suffering from some other disorder, so that colitis of one form or another more often called for treatment. Next comes the inflammatory complication of diverticulosis, namely diverticulitis, of which there are 120 cases, and then growth of the colon, which was just about half as frequent as diverticulitis.

At the bottom of the list, but not counted as a disease, there are 1,520 cases of delay in the colon, proved radiologically, and 304 cases of ptosis. These two figures are from complete X-ray examination of the alimentary canal of over 5,000 people.

The *age incidence* of a large group of these diseases is set forth in Table II.

TABLE II

				Average age	
				Cases	Years
				Per cent.	
Colon dropped	M. 104	34.2	45.2
			F. 200	65.8	41.6
			M. and F. 304		42.8
Colitis	M. 210	40.5	48.1
			F. 309	59.5	42.9
			M. and F. 519		43.8
Colon delay	M. 733	48.6	49.1
			F. 744	51.4	44.2
			M. and F. 1,477		46.6
Diverticulitis	M. 369	67.3	59.4
			F. 179	32.7	55.2
			M. and F. 548		58.2
Diverticulosis	M. 75	89.3	62.4
			F. 9	10.7	57.8
			M. and F. 84		61.9
Cancer	M. 47	73.4	64.0
			F. 17	26.6	57.0
			M. and F. 64		62.0

The average ages fall in the twenty years from the forties to the sixties.

I shall refer briefly to-day to a few selected aspects of interest of the main groups in the order of the age at which they occur.

Table II shows also the *sex incidence*. There were two women with ptosis of the colon to one man, three women with colitis to two men, and a nearly equal number of each with constipation, when proved radiologically—a surprising figure, for it is generally assumed that constipation is far commoner in women than in men.

In the later ages the disorders of the colon are commoner in men, the proportions being: diverticulosis twice as common, diverticulitis nine times, cancer three times as common in men as in women.

GENERAL DIAGNOSIS

In the general diagnosis of diseases of the colon, come first and foremost the history, the study of symptoms, and the clinical examination. Many mistakes are still made in practice by omitting to examine the faeces and rectum. The sigmoidoscope is a valuable aid. With proper preparation, including $\frac{1}{4}$ gr. of morphia, and with gentleness and skill, it can be passed without severe discomfort. The use of

barium and X-rays has added the most valuable experimental measure we have. In this department I have had the advantage for many years of the collaboration of Mr. O. A. Marxer. The whole colon can be demonstrated with a proper technique. Fore and aft pictures are not enough; each loop should be seen in profile. The barium enema is more helpful in most cases if preceded by a barium meal, for the enema does not show the segmentation of the bowel or certain other details so well as the meal, nor the rate of passage. In cases of doubtful narrowing, air inflation will expand a spasm, but not an organic stricture. There is one area in which it is sometimes difficult to show the shape of the lumen by X-rays, namely the recto-sigmoid junction. This can be inspected by the sigmoidoscope.

Flatulence.—It is necessary to find out what the patient means by speaking of "flatulence". The word is commonly used to denote (a) Eructation from the stomach of wind; (b) its passage by the bowel; (c) the unsuccessful desire for (a) or (b); (d) distension; (e) a feeling of distension, which is not evident on examination; (f) borborygmi, with or without any of the above. Aerophagy is sometime diagnosed when belching is due to an attempt to get rid of a distress or pressure, and there is but little air in the stomach. Dilatation with gas or other material causes more distress in the small than in the large intestine. The retention of gas in the colon is due to interference with the normal movements, and the blood supply. It is suggested [13] that if the bowel does not execute its continual slow movements, the venous blood is not passed on, soon becomes saturated with any gas present, and cannot take up more. It is improbable that much gas, except in certain rare conditions, is from abnormal fermentation.

As the blood supply becomes less with arteriosclerosis, there tends to be an increase of flatulence, which is therefore a normal accompaniment of advancing age. In some it may, from this cause, become distressing and need vigorous treatment.

Dropping of the Colon.—The healthy bowel can be said to float in the abdomen, the mesentery being "more a guy-rope" than a support [12]. Sherrington showed that the afferent splanchnic nerves from the bowels throw, reflexly, the abdominal muscles into tonic contraction, and this happens when we stand up. If the mechanism fails the bowels lie lower in the abdomen. The bowel muscle generally shares in the poor tone of the abdominal muscles, but not always. In true ptosis the flexures are dropped, the hepatic the more of the two. The top of the bend must be seen; it may be filled with gas. In a series of 200 cases observed by Mr. Marxer, consisting of nearly equal numbers of colons which were (a) normal in position, (b) partially dropped, or (c) much dropped, delay was not appreciably commoner in colons which were dropped than in those in a normal position; indeed, in more than half of the cases of ptosis there was little or no delay. In patients with much ptosis and constipation the real disorder is the general loss of nervous and physical tone, and the cause does not lie in the position of the bowel. It does not matter where the colon is, so long as it has the power to fulfil its duties [2], and when that power has been lost it may be regained by suitable treatment without alteration in position.

Constipation has been investigated statistically by my colleague, R. P. Picton-Davies. In 10% the complaint of constipation was not justified, the rate of passage both of charcoal and of a barium meal being normal. In 1,000 cases in which there was real delay shown radiologically, in half the whole colon was involved, in a third the sigmoid and rectum, and in 11% the rectum only [13]. Nearly a quarter of the 1,000 patients were unaware that they were constipated, and of these nine out of ten had no other disorder referable to the colon.

The colon, except the distal part, is naturally full, not empty. The faeces are so mixed that they contain the residues of two or three days together. A reasonable delay is a function of the colon. The distal part should enter into extrusive movements only upon the stimulus of faeces in the rectum with the attempt at defaecation. Failure of defaecation is not usually due to weakness or paralysis of the bowel muscle

as patients often think, but, apart from general disease, to undue drying and hardening of the fæces, absence of the normal stimulus, rectal sensation having become dulled from neglect, or to the irritation or pain of some local lesion, usually piles. Extrinsic lesions also may have a similar effect. Since a purge empties the residue of two or three days [12] it would seem reasonable not to repeat it for that length of time.

Treatment should aim at restoring the natural reflex by removing local disease or irritation of the anus or rectum, by securing an unhurried daily effort at an appropriate time, making sure that the rectum is emptied daily, using a stimulus if needed of the rectum itself, e.g. a suppository or small enema, and by the use of a little, not too much, paraffin.

Paraffin is a harmless laxative, but sometimes an uncomfortable one. If taken in large doses there are many in whom much gurgling and unpleasant wind follows, and leakage. Its valuable rôle is as a lubricant. By its use the residues can be prevented from becoming hard, so that a motion can be passed out with a normal effort. A teaspoonful or a dessertspoonful in water night and morning is often enough. The analyses of A. J. Leigh [15] have shown that paraffin does not, as at one time suggested, prevent the normal absorption of food.

The general discomfort of constipation is often ascribed to poisoning. The relief after a motion is too rapid for that to be true. The symptoms are probably mainly due to simple distension, for if cotton-wool or a balloon is introduced into the rectum it is found that in sensitive persons nausea, "dopiness" and depression are induced [12]. Nevertheless it can hardly be believed that all the results of constipation are mechanical; and since absorption of toxins can take place in severer diseases, we must allow that there may be a less degree in the milder ones, e.g. in what I have called "purgative colitis".

The cæcum is not a cesspool by nature, though sometimes made one by art, nor is a moderate constipation necessarily harmful. Frequent purges are undesirable; they are a cause of diminished vigour of the intestine, and in some of poor health.

The diagnosis of *intestinal auto-intoxication* must be regarded with suspicion. In 90 cases admitted to our clinic [13] with a diagnosis of intestinal auto-intoxication 32 were suffering from organic disease, such as peptic ulcer, 8 cases, diverticulitis 7, cholecystitis 6, syphilis 3, rectal growth 2, and others from heart disease, nephritis and gout. When these and the neurasthenias from various stresses were separated out, a few cases remained in which the bowel, apart from organic disease, could be regarded as the cause of the symptoms. Intestinal auto-intoxication as a diagnosis in vague cases has now a strong popular rival in endocrine deficiency.

Redundancy of colon.—142 redundant sigmoid loops were noted in about 5,000 X-ray examinations, just under 3%. Are these redundant colons to be looked upon as congenital, like Hirschprung's disease, or acquired, or in part congenital, developing with age? X-rays show that when the bowel relaxes it becomes longer as well as wider. And the deficient shortening on evacuation in some of these cases suggests that with years of constipation the affected part would tend to get longer and longer. I suspect that that occurs, but hardly enough time has passed since accurate X-ray observations began to be made to prove the point. In our series a redundant sigmoid is commoner after 50 years of age than before 30.

Unless there is organic obstruction, operations for constipation, though they have their successes, have more often failed; and some of them have been disastrous to the well-being of the patients. It has been found better, after many trials and errors, not to excise more than the necessities of the case demand. In the rare cases of great redundancy which fail to respond to a prolonged course of medical and physical treatment, controlled by X-ray observations, and in which the bowel does not shorten on evacuation, a judicious short-circuit may be helpful.

Sympathectomy, which has an established place in the treatment of Hirschprung's disease [8], has not, as a rule, conferred lasting benefit in chronic constipation. This is the opinion of Professor Learmonth and is confirmed by our experience.

Volvulus.—From the redundant sigmoid, which is fairly common, there being 142 cases, we pass naturally to the cases of volvulus, which are rare—9 in this series. The diagnosis of volvulus of the sigmoid, which is the part affected in three out of four cases, is sometimes not difficult, with the complete obstruction, drum tightness of the lower abdomen and, at first, less constitutional disturbance, and especially less vomiting, than might be expected. There may be also a history of former attacks. Relief may be obtained from posture and enemas and, if it comes, is dramatic.

Attacks of partial volvulus are less easy to recognize and may puzzle a succession of doctors, until this diagnosis is thought of, usually, in my experience, with the help of the radiologist. Some such cases can recover and keep well with medical treatment, similar to that for constipation. If the loop is emptied regularly it may become smaller and less likely to twist. If recurrence takes place operation is advised. Volvulus of the cæcum, or ileocaecal junction, of which there were two cases, is more obscure but less severe.

Colitis

Full physical and psychical examination is important in cases diagnosed as *mucous* or *mucomembranous colitis*; for in many of these the circumstances of the patient, constipation, and co-existing lesions are preponderating factors. A laparotomy is not at the present day, except in emergency, an intelligent method of diagnosis, though it should be used without delay if there is a reasonable suspicion of serious disease. It is better as a rule to investigate first and operate afterwards. The same applies to medical treatment. It is not a good plan, when symptoms are well established, though it is tempting, easy and prevalent, to try a course of treatment first and then, if it fails, to investigate. The patient is pleased to begin with. He likes his doctor to do something. But later, if investigation reveals something which might have been found weeks or months before, his feelings change.

In the treatment of mucous colitis, the calm which follows a diagnosis made after a careful investigation, the confident discussion and ventilation of circumstances and difficulties, a complete change, a sensible régime of food, and the initiation of a normal habit of bowel are as important as the physical and medicinal aids that are also used [13]. The disease has become less common of late. This may be ascribed to the effect of teaching the harm which follows daily purgation, and to the greater use, by all classes, of greens and fruits.

Ulcerative colitis.—The chief advances in treatment that have been made in my time are (1) that a reasonably nourishing diet is now given, as I have for many years advocated. Mr. Lockhart-Mummery also put forward this view cogently. There are a few cases that do better on milk and it is wise to try different foods in resistant cases. One severely ill man, whose case has been published [14], recovered upon a régime of sieved beef. (2) Intestinal douching should be gentle, at low pressure, with bland fluids. Every other day is usually enough. (3) Any anal or rectal lesion should be treated at the earliest possible moment. (4) Prolonged and repeated search for *Entamoeba histolytica* should always be made. It was found after months or years in 5 out of 56 cases.

Bacteriological methods of treatment, whether by vaccine or by sera, have proved disappointing. Some, however, still report good results with a thorough application of antidyenteric serum as recommended by Hurst. A 60% recovery is reported in one series of 64 cases treated by Dr. J. R. Bell [1] in Australia. In that country Shiga dysentery is commoner than it is here. And the Commonwealth antidyenteric serum, the basis of the preparation of which was laid some years ago by W. J. Penfold and S. W. Patterson, contains the antitoxins of Shiga and Sonne groups; also immune bodies against numerous Flexner strains. In this country the antidyenteric serum is sometimes prepared from the Shiga bacillus. If the patient has not had an initial Shiga dysentery any benefit is likely to be due to non-specific protein therapy. The mortality does not appear to be less than that of other methods of treatment. But that does not dispose of the question whether those who succumb without the serum

treatment might not have recovered with it; for recovery is reported in some advanced cases. The vaccines and sera of Dr. Bergen are prepared from diplococci obtained from the subjects of the disease. They have probably had a more extended trial than antidyenteric serum, but agreement as to benefit has not been attained.

Most cases in a clinic with daily care recover—I say this with knowledge of the high mortality of general hospitals. Our mortality has been 16%. The fatal cases, if the patients were not too ill on admission, and if reasonable time was available for treatment, leave behind the question—could anything different or better have been done, such as an appendicostomy, to wash through the colon or an ileostomy, with a large catheter leading to a rubber tube, to take away all the faeces from the colon. I have seen benefit from each of these procedures. If one or other is contemplated it is better done early than late.

After-treatment.—Those who have recovered from an attack of ulcerative colitis should live a careful life with simple food and regular rests, avoiding fatigue and strain, and so far as possible, the risk of infections. The disease, like peptic ulcer, is liable to recur; but I have seen many patients remain well over long periods up to the present. I have also seen recurrence follow overwork, emotional stress, the drinking of beer, which was known to disagree, colds, pregnancy, and the omission of a weekly douche.

Diverticulosis and Diverticulitis

The average age of the patients was 58 years, fourteen years above that of those who had colitis.

The term diverticulitis should be reserved for the disease to which it was first applied, namely, the state in which inflammatory changes have occurred round the pockets, involving the intestinal wall and, later, adjacent structures. This distinction, which I made many years ago, still needs to be mentioned because, if a few pouches are seen on a film, the patient is even now sometimes reported to be the subject of diverticulitis, a more serious disease.

The word sac is shorter and, I am assured, classically more respectable, than the word diverticulum. From it, we should get the words *saccosis*, *saccitis*, of the colon, with the adjectives *saccal*, *presaccal*, terms which I prefer. But to alter medical nomenclature is difficult, even to substitute a shorter and more scholarly term.

Mr. Marxer first observed the pre-diverticular appearance in 1920. We have now noted this state in 132 out of 564 consecutive cases of diverticulosis. Two points are to be observed, (1) the fine concave depressions in profile, (2) deformity of the curved outline of the haustrum.¹ When the pouches are formed, not only do the fine corrugations disappear, but the normal outline of the haustrum is restored.

The pre-diverticular state appears to be caused by local spasm of groups of muscular fibres. If the whole circumference is involved there is constriction. The area affected is often small; a large area is, however, occasionally involved, with much pain and disturbance. This is rare, but I have known the abdomen opened in two instances, redness of the intestine being observed. Sir Charles Gordon-Watson has described a similar case.

Diverticula have been supposed to be simple pulsion pouches. But the deformity of the haustrum, which may be considerable, is not easily explained on the view that at a few weak places lining membrane is being passively extruded by pressure from within. Also fresh patches of the pre-diverticular state occur, sometimes at long intervals, in different loops or at different parts of the same loop, in which the conditions of pressure and structure may be thought to be the same. And when an area of diverticulitis becomes exacerbated, and clinical symptoms recur, new patches in the

¹ A radiogram was exhibited showing the progress from this state to the formation of diverticula in a patient observed over nine years.

pre-diverticular state are often found near to it both above and below the inflamed swollen area. Further, douching with saline and the use of paraffin are often followed by a lessening or even disappearance of the pre-diverticular patches. Such observations suggest that there is some preceding process, probably inflammatory, which determines the site at which pouches will develop. The chances of obtaining material by biopsy or post-mortem from the exact area are few. From sections examined so far there was in the pre-diverticular area an excess of small white cells as compared with the normal; but the material is too scanty to draw a histological conclusion.¹

When the pouches are formed, if they fill and empty normally there is no reason why they should become inflamed, and they may be quiescent for many years, or until the end of life. If, however, material is not discharged through the narrow neck, then a faecolith is formed. It is from the necks of these lith-containing diverticula that inflammation appears to spread into the bowel wall, setting up diverticulitis [17]. As soon as a considerable area of the wall is involved it ceases to contract and relax, and its fixed state can be demonstrated by radiology, especially by superimposing tracings of serial films. By that time, intermittent symptoms of inflammation in the left iliac fossa occur: Discomfort, pain, dragging, and backache. A tender tumour develops, and in worse cases there will be malaise and fever. Constipation is usual, but diarrhoea may occur. Untreated cases go to hardening of the whole bowel wall and gradual narrowing, with constipation and later spread of the inflammation to adjacent structures. The pouches become involved in the mass and all trace of them may disappear. With X-rays a typical fixed palisade appearance is seen [17, 18]. This type forms many of the advanced insidious cases of chronic diverticulitis.

I should like to stress the importance of recognizing another class of case, which is acute in its clinical onset and yet more amenable to treatment by douching, careful diet, and paraffin. In this the inflammation may affect, at first, mainly the mucous membrane and if the lining becomes oedematous it may cause at an early stage partial or complete obstruction. Thus sudden obstruction in diverticulitis is often due to swollen mucosal folds [18].

The swollen mucosal folds may form polypi. There were 16 such cases. Several of them had no special symptoms. Others were associated with obstruction as above mentioned, and two with hæmorrhages. In a case of polypus at the splenic flexure, there was alarming colic, with distension. The symptoms ceased with douching and paraffin. After two years the patient omitted treatment and there was recurrence, treatment being resumed with success.

The principles of treatment in the early stages of a diverticulitis are (1) to keep the motion greased with a little paraffin. A teaspoonful or a dessertspoonful night and morning is often enough. (2) To douche gently with saline every 2-7 days. (3) To give a diet with some sieved or well-chewed fruit and greens. (4) To avoid bowel irritation from rich foods, and too much alcohol. And (5) to live a hygienic life without over-fatigue. Some advocate the avoidance of fruit and greens, and the use of purges throughout. But it is clear from study of the way in which the pouches empty [18] that it is better, so long as it is possible, to maintain the natural activity of the bowel muscle. In some advanced cases purges, such as salts, are needed at regular intervals, and when there is inflammation of the mucous lining the diet must be a bland one, as in other forms of colitis.

In a few instances, but only a few, a diverticulitis is localized and can be excised.

¹ The recent paper in the *British Medical Journal* (1937) (i), by D. M. Lubbock, W. Thomson and R. C. Garry on "Epithelial Overgrowths and Diverticula in Rats fed on a Human Diet" raises the possibility that the development of diverticula may be associated with deficiencies in diet, in so far as the diverticula observed in rats are comparable with those occurring in man. These authors support the view that mechanical causes are not enough to explain the development of multiple diverticula in the colon. They also support the writer's experience that in the early stages of diverticulosis an ample lactovegetarian diet is desirable.

There must be enough normal, or at least non-inflamed, bowel above and below the affected part. I have seen three such cases, all successful, the first of which was operated on by Mr. Lockhart-Mummery.

Efforts should be directed to earlier discovery of the disease, so that fewer cases may be allowed to progress to the deplorable final stages. As soon as it is discovered diverticulitis should be treated thoroughly, for the inflammation may, and often does, progress without a symptom. After an attack has been successfully treated the area should be examined by means of a barium enema every few months at first and should never be left unexamined for more than a year.

Cancer of the colon

Last in the series, in the order of age, comes malignant growth of the colon. The average age in 64 cases was 62 years. But the range is wide, from 39 to 92. Most, however—indeed five out of six—were between 50 and 70 years of age. There were three men to one woman, and in more than half in each sex the growth was in the sigmoid.

In an analysis by S. W. Patterson [11] of the above cases there were *four* main types of onset:—

(1) Bowel disturbance, 36 cases. In half of these the complaint was constipation and in the other half irregular bowels or diarrhoea—the “colitic onset”.

(2) Pain, 17 cases, usually related to the growth, or to the active bowel above it.

(3) Discomfort in the upper abdomen, or nausea, 11 cases—the “dyspeptic onset”. In one patient much time had been lost by a course of treatment for a supposed duodenal lesion. The lesson the dyspeptic cases teach is that when examining with a barium meal, it is well to watch it through the bowel and give a barium enema. Many patients claim to have been X-rayed with barium in whom only the stomach and duodenum have been observed. The one examination is, of course, over in a few hours, whilst the other may extend over three or four days. The chance of there being a growth of the colon is small; but, if present, its early recognition is of overwhelming importance. Further, other colonic disorders may be found which are contributory to the dyspepsia.

(4) The first sign, in 11 cases, one in six, was the passage of blood from the rectum. Blood was passed at some time in about two-thirds. In seven cases neither blood, mucus, or pus was detected in the faeces on macro- and micro-scopical examination. It is presumed that in these there was no ulceration of the lining of the bowel.

In the clinical *diagnosis from diverticulitis*, the following points are in favour of that disease: A long, but intermittent, history of discomfort, maintenance of weight, healthy appearance, much tenderness, fever, sudden obstruction. The opposite, namely an uneventful deterioration with bowel disturbance, but only gradual obstruction, is more likely to be produced by growth.

Diverticulitis and cancer were found together in six cases. We have the impression that this association is not commoner than would be explained by the frequency of the two diseases. Indeed, when we think of the association of irritation and malignancy it is surprising that more cases of diverticulitis do not become cancerous.

Excision is, in a proportion of early cases, successful. In this series the length of history ranged from a week to three years. The average time since the first symptom had called attention, in 55 cases in which the history, as related, seemed to be accurate, was eleven months. More lives could be saved if that time were shortened. All patients presenting unexplained symptoms should be examined carefully as soon as possible, before severe illness supervenes. Thirty-eight patients came to operation. In two nothing could be done. In nine a short circuit, and in 14 a colostomy or caecostomy was done. In 13 only was excision possible, and was successful in 8. Two of these were alive more than ten years later. Dixon and Olsen [3] have recently recorded 12 cases of survival over twenty years after operation. The nature of the

tumour, that is, its rapidity of growth and dissemination, is more important as regards prognosis than the completeness of the obstruction. Thus great dilatation above is compatible with successful operation.

In conclusion : In trying to practise the combination of careful clinical study—which must always come first—with scientific methods of diagnosis, it becomes clear that much mental and physical suffering may be avoided by early and adequate examination in cases of doubt.

I have been speaking mainly of the objective signs of disease, but it is especially important in disorders of the colon to give time and care to consider the man, or the woman, as well as the lesion—the mind as well as the body.

[The paper was illustrated by radiograms shown on the epidiascope.]

REFERENCES

- 1 BELL, J. R., Communication to Brit. Med. Assoc., Melbourne, 1934.
- 2 DAWSON, LORD, *Brit. M. J.*, 1921, (ii), 31.
- 3 DIXON, C. F., and OLSEN, P. F., *Surg., Gynec. and Obst.*, 1936, 874.
- 4 HURST, A. F., *Lancet*, 1935 (i), 1489.
- 5 Id., *Guy's Hosp. Rep.*, 1935, 85, 317.
- 6 LOCKHART-MUMMERY, P., "Diseases of the Colon", London, 1931.
- 7 MANSON-BAHR, P., *Lancet*, 1936 (i), 759 and 830.
- 8 MORGAN, C. NAUNTON, *St. Barth. Hosp. Rep.*, 1933, 66, 22.
- 9 NIKLAS, F., *Klin. Wchnschr.*, 1926, 2, 2216.
- 10 PATTERSON, S. W., *Med. Press and Circ.*, 1937, p. 332.
- 11 Id., *Brit. M. J.*, 1937, (i), 882.
- 12 RANKIN, F. W., BARGEN, F. A., and BUIE, L. A., "The Colon, Rectum, and Anus". Philad. and London, 1932.
- 13 SPRIGGS, E. I., *Quart. J. Med.*, 1931, 24, 533.
- 14 Id., *ibid.*, 1934, 28, 549.
- 15 Id., *Lancet*, 1930 (ii), 992.
- 16 SPRIGGS, E. I., and MARKER, O. A., *Proc. Roy. Soc. Med.*, 1920, 13 (Sect. Surg. 65, Sub-Sect. Proct.).
- 17 Id., *Quart. J. Med.*, 1925, 19, 1; *Lancet*, 1927 (i), 1067.
- 18 Id., *Brit. Encyclop. Med. Practice*, London, 1937.

Discussion.—MR. LOCKHART-MUMMERY said he had noticed that in a few cases ulcerative colitis had been present in two generations of the same family, and this made him suspect that there was some hereditary diathesis towards infection of the colonic mucosa. He had known a case of recurrence of colitis following extraction of a septic tooth. This, it seemed to him, was proof that the sepsis from the teeth was an important factor in causing the recurrence of the ulceration.

He agreed with Sir Edmund that one must be very careful to exclude cases of chronic amœbic dysentery, as they were most deceptive. He had been deceived on several occasions in spite of repeated tests of the stools for parasites and cysts. He believed that, if there was any doubt, the best practice was to give emetine.

DR. G. E. VILVANDRÉ said that in his experience the diagnosis of early growth of the colon was difficult in some cases. It was easy enough to show a large carcinoma, but this was really of little help. It was the early stages that were important, and the more he saw of such cases the more he was convinced that any radiological abnormality should be confirmed by the sigmoidoscope; he would go further, and say that a negative X-ray report should not eliminate clinical suspicion. Here again sigmoidoscopic examination should be made when the lower portion of the bowel was concerned. He had known of carcinoma of the rectum not revealed by X-ray examination and yet readily felt when a digital examination was made. This examination should never be omitted, and it was the radiologist's duty to find out whether it had been performed by the practitioner and, if not, to carry it out himself.

SIR ROBERT ARMSTRONG-JONES, speaking with regard to the frequency of abdominal symptoms in association with mental disease in his past experience at Claybury, said he had known volvulus to have occurred, also appendicitis, and on several occasions strangulated hernia, but he thought that such occurrences were infrequent, indeed, he thought that appendicitis was less frequent, in proportion, among the patients than among the staff.

[March 10, 1937]

Meckel's Diverticulum causing Severe Recurrent Hæmorrhage from the Bowel.—W. B. GABRIEL, M.S.

History.—A. C., male, aged 22 in 1936. First attack of melæna in May 1934; lost half a pint of blood repeatedly, and was in hospital for some months before coming under my observation. In August 1935 had a slight attack of hæmorrhage and was in bed for a week.

May 1936: Severe and prolonged hæmorrhage. In-patient in Royal Northern Hospital from May to August. Pulse up to 130. Two blood transfusions given. At one time the red blood cell count was down to 1,900,000, and the hæmoglobin to 25%. He never had any pain during the attacks, and the abdomen was always soft and free from tenderness. Later in 1936 a barium meal test was carried out with negative results, no duodenal ulcer being revealed.

The last attack of bleeding occurred on December 31, 1936. The patient had a sudden attack of tenesmus and passed about 5 oz. of dark blood.

Operation was accordingly decided upon, with the object of exploring (1) the duodenum, (2) the lower ileum, for a Meckel's diverticulum, (3) possibly the colon, for a cavernous angioma.

Operation (13.1.37).—The abdomen was opened through a right paramedian incision; the duodenum was explored and found to be normal. The cæcum was next delivered, and the small intestine examined backwards from the ileo-cæcal junction. At a distance of about 2 ft. a large Meckel's diverticulum was delivered; it was about 3 in. in length, the tip being unattached to the abdominal wall, or to any other structure; it was dark in colour and appeared to contain blood. Coming up from the mesentery there was a very large pulsating artery much bigger than any neighbouring vessel. In view of this unusual blood supply, I decided to resect the affected segment of small intestine, which was accordingly done, the continuity of the bowel being restored by a lateral anastomosis.

The patient made a good recovery. He is now very well and the secondary anaemia has completely disappeared.

Pathological examination.—In the recent state the Meckel's diverticulum was about 3 in. in length, and $1\frac{1}{2}$ in. in diameter (fig. 1). A hard, slightly irregular nodule was present at the tip and on bisecting the specimen this was seen as a solid white tissue beside which was a small ulcer. This can be easily seen in the accompanying photograph (fig. 2) together with the cut surfaces of several large vessels at its base.

Microscopical examination.—The solid tissue is proved to consist of pancreatic tissue with a few islets of Langerhans. The adjacent portion of the mucous membrane is ulcerated and shows signs of acute inflammation; it resembles gastric mucosa, and large blood-vessels, probably arteries, are seen in the submucosa beneath the ulcers.

Commentary.—In this case the bleeding was clearly proved to have originated from an ulcer in a Meckel's diverticulum. The case appears to be a classical one of this type and attention is drawn to the paper by Chesterman [1] in which four new cases were reported, together with a bibliography relating to hæmorrhage as a complication of a Meckel's diverticulum.

Reference.—CHESTERMAN, JUDSON T., *Brit. J. Surg.*, 1935, **23**, 267.

Mr. HOPE CARLTON mentioned a case in which he had removed the Meckel's diverticulum by transverse section at its base, after which there appeared to be some narrowing of the small intestine at the point from which the diverticulum had sprung.

This was in accordance with the cases related by previous speakers. He therefore resected the affected loop and the patient had made a normal recovery.



FIG. 1.

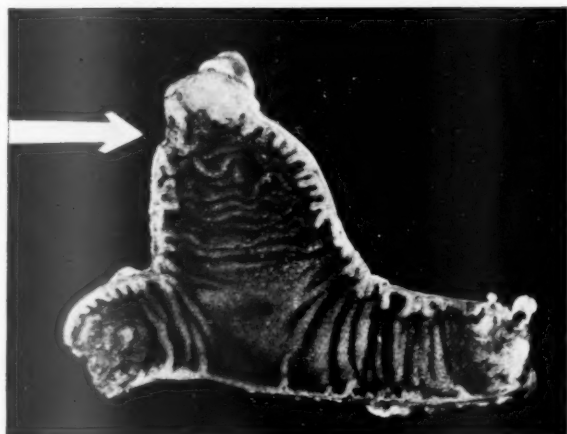


FIG. 2.

Angioma of the Rectum.—W. B. GABRIEL, M.S.

The patient, W. B., an errand boy aged 19, was sent up to me by Mr. H. S. Taylor-Young, of Salisbury, with a diagnosis of cavernous angioma of the rectum. Since 1921 he had been admitted on five occasions into hospital for treatment of secondary anaemia due to hæmorrhage from the bowel: the red blood cell count had been down to 1,200,000, with 15% of hæmoglobin.

On admission (St. Mark's Hospital).—A pale youth; red cells $3\frac{1}{2}$ millions, hæmoglobin 45%, colour-index, 0.6. When he strained down, what appeared to be a

large, soft, deeply-congested pile was seen in the right posterior anal quadrant, with a very unusual extension of venous engorgement externally. On digital examination an unusual degree of pulsation was noted under the mucous membrane in that quadrant.

Operation.—April 16, 1936, under local anaesthesia: The affected segment of rectal mucosa was dissected up with scissors, and ligated at its upper pole by Goodsall's method, without undue hæmorrhage taking place. The external part was excised, leaving a flat wound, which was dressed with gauze and attended to subsequently as for a case of piles.

The patient made an uneventful recovery, and two weeks later the red blood cell count had increased to $4\frac{1}{2}$ millions, and the hæmoglobin to 70%. He was discharged home on the twenty-sixth day after operation. When seen as an out-patient, two months after the operation, he looked pink and well; hæmoglobin, 85%; red blood cells $5\frac{1}{2}$ millions. The anal scar was quite smooth and there was no sign of angiomatous tissue. Since then he has remained in good health, and has been back at full work.

Section of Urology

President—BERNARD WARD, F.R.C.S.

[April 22, 1937]

The Harris Operation and its Modifications

By CLIFFORD MORSON, O.B.E., F.R.C.S.

THERE are three diseases of the prostate for which prostatectomy by the Harris technique, with its modifications, is indicated. They are adenomatous disease, fibromyoma, and chronic prostatitis with calculus formation. The first condition is common, the second rare, and the third by no means infrequent. In this last disease the whole prostate is removed, in the two former the pathological mass is enucleated from within the gland.

The preparation of the patient for prostatectomy is well known, and is no different for the Harris technique from that for any other. The details of this technique as I practise it for adenomatous disease are as follows :—

My assistant passes a catheter and washes out the bladder with 1:8,000 oxycyanide of mercury, and then distends it with about 10 oz. of the lotion. He then withdraws the catheter and applies a penile clamp. The next step is to divide the vasa deferentia just below the external abdominal ring. This is done by separating the duct from the rest of the cord with the finger and thumb, and holding it immediately beneath the skin. An incision through the skin exposes the vas, which is pulled out of the scrotum with a pair of toothed forceps. It is then divided. By this procedure the surgeon ensures that his patient will not develop epididymitis during the post-operative convalescence.

Infection of the vesiculæ seminales is a frequent occurrence prior to operation, and is due either to bacteriuria or urethral instrumentation. The next step therefore is to sterilize these organs by irrigation, which can be accomplished by injecting an antiseptic into the proximal end of the cut vas, about 10 c.c. of 1:60 carbolic acid being used for this purpose.

The next step is to place the patient in the Trendelenburg position and open the bladder by a vertical sub-umbilical incision. The contents of the bladder are previously evacuated by my special trocar and canula, to which is attached a long rubber tube which siphons out the fluid. Expensive suction machines are not needed. Enucleation of the adenomatous mass follows and is carried out by the intra-urethral method recommended by Harris, but without the finger in the rectum. It should be performed rapidly and the tumours removed as a whole—not in pieces—in order to minimize hæmorrhage. As much of the prostatic urethra should be preserved as is possible. The larger the intra-vesical projection, the more prostatic urethra can be left behind. The reason for this I described in my address at Melbourne in 1935.

After the main tumour mass has been removed it is important to palpate the shell of prostatic tissue which forms the so-called prostatic bed, in order to feel for isolated adenomata. These if not enucleated will grow and eventually cause a recurrence of the pre-operation symptoms.

The illuminated bladder retractors are now placed in the bladder and the entrance to the prostatic cavity is visualized. On no account should tags of mucous membrane be cut away. I entirely disagree that their retention increases sepsis. They are

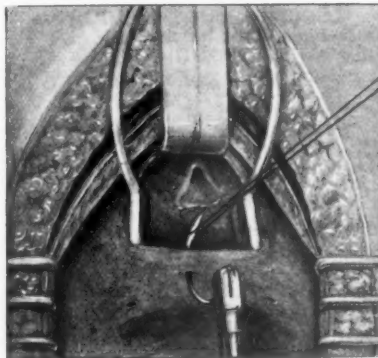


FIG. 1.—The anterior illuminated retractor with the prostatic speculum is seen in position. The prostatic bed and the torn end of the prostatic urethra are visualized. The boomerang needle has been passed through the mucous membrane of the trigonal flap and the catgut suture attached to it.

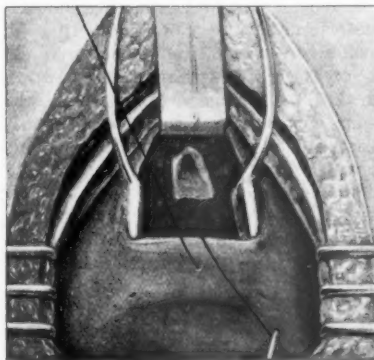


FIG. 2.—To show the first manoeuvre of the trigonal flap suture.

valuable grafts for covering up the raw surface of the lateral walls of the prostatic cavity.

The next step is to insert the anterior illuminated retractor with the speculum attachment. The walls of the cavity are thus separated and bleeding is temporarily controlled. A good view should be obtained of the floor of the cavity and possibly of the torn end of the prostatic urethra. The trigonal flap is now sutured to the prostatic bed and drawn as near to the urethral mucous membrane as it is possible.

In a few cases the bladder and the urethral mucous membrane can be brought into apposition. Only one suture is used and it is inserted so that there is no subsequent retraction of the trigonal flap (figs. 1, 2, 3, and 4). The post-prostatic pouch is entirely obliterated by this manoeuvre. Harris used three sutures for this part of the technique, a postero-median and two postero-lateral which he called hæmostatic. The latter I have discarded because they may occlude the ureteric orifices, as was proved by post-mortem examinations on two of my cases.

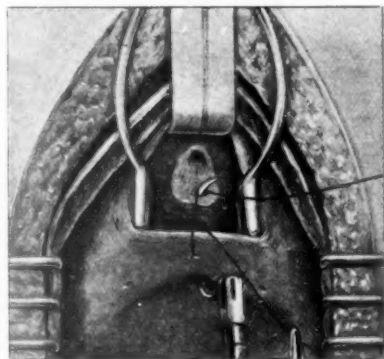


FIG. 3.—To show the second manoeuvre of the trigonal flap suture. The needle has been passed through the whole thickness of the trigonal flap, the prostatic tissue forming the bed, and the torn mucous membrane of the urethra. The needle is threaded with the flap suture.

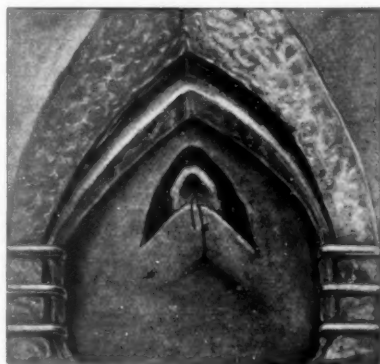


FIG. 4.—The trigonal flap suture has been tied. Note that retraction of the flap is impossible.

A 22-French-size rubber Malacot catheter with two eyes is now inserted into the urethra by means of a metal introducer and brought out into the bladder. A silkworm-gut suture is passed through this catheter, immediately distal to the second eye, and a pair of artery forceps is attached to each end. The mushroom top is cut off with scissors, thus allowing for better drainage. This is followed by the insertion of

my figure-of-eight stitch into the lateral walls of the prostatic cavity (fig. 5). This stitch has a threefold function. Firstly it acts as a hæmostatic, secondly it infolds the mucous membrane of the lateral walls, so that the raw surfaces are in contact, and thirdly it reduces the space between the reconstructed internal meatus and the triangular ligament. The importance of this stitch, and of the one binding the trigonal flap to the prostatic bed, cannot be over-estimated, as will be shown when

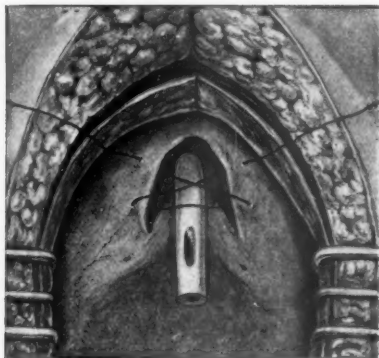


FIG. 5.—The urethral tube in position after the posterior stitch has been tied. The figure-of-eight suture has been inserted. (The knots in the trigonal flap are incorrectly drawn and can be ignored.)

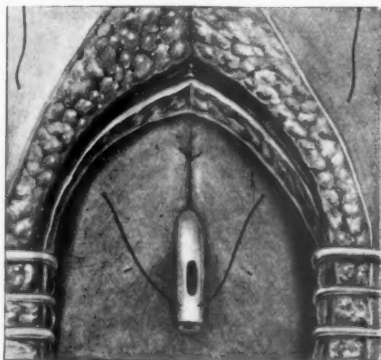


FIG. 6.—The figure-of-eight stitch has been tied. A suture has been passed through the catheter and lateral walls of the bladder and abdominal wall. (The anchoring stitch for the urethral catheter.)

the post-prostatectomy complications of other techniques are considered. All clots are next removed from the bladder and the new internal meatus is visualized. It has two striking features—firstly it is on a level with the base of the bladder, thus entirely obliterating the post-prostatic pouch, and secondly it closely resembles the appearance of the internal meatus in a normal bladder neck (fig. 6).

The illuminated bladder retractors are now dispensed with, and the surgeon proceeds to pass the silkworm-gut suture, holding the catheter in position, through the bladder and abdominal walls and out through the skin. Care must be taken not to puncture the deep epigastric vessels with the needle, by keeping close to the cut edges of the skin.

The next step is to close the anterior wall of the bladder, but primary closure must only be practised if the urine before operation is sterile and the surgeon is sure that he has controlled the bleeding of the lateral walls of the prostatic cavity (fig. 7). Therefore the contra-indications of primary closure are infective pyelonephritis, severe cystitis, and inadequate hæmostasis. In these cases a small angular White's tube suffices to assist in bladder drainage.

It is wise, with primary closure, to drain the pre-vesical space by means of a corrugated rubber wick. A slight leakage of urine is always a possibility, but will cause no trouble if there is a vent for its escape. Lastly the ends of the silkworm-gut suture which maintains the catheter in its correct position are immobilized by metal buttons of the Emesay pattern.

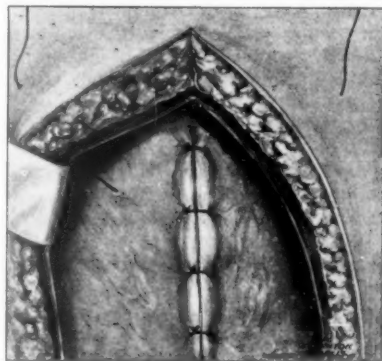


FIG. 7.—The anterior wall of the bladder completely sewn up. The anchoring stitch can be seen protruding through the skin of the abdominal wall.

Before the patient is returned to bed the bladder should be irrigated through the catheter. The after-treatment recommended by Harris is strictly adhered to, except that so long as the catheter is retained in the urethra the patient is nursed on an inclined plane, the head of the bed being raised about 2 ft. from the ground. This should be done immediately the patient is returned to the ward. Not only does this position assist drainage from the bladder, but it adds enormously to the comfort of the patient. It is possible too that the danger of pulmonary embolism may be avoided by adopting this procedure.

The catheter is attached to a special glass urinal which has been made for me by the Genito-Urinary Manufacturing Company. It is instructive to note how little discomfort is caused by the presence of a soft rubber catheter in the urethra, maintained in position by the technique which I have just described. This is an important step forward in adding to the comfort of the patient during post-operative convalescence. The degree of urethritis is negligible and the catheter, so long as the

NOTE.—Figs. 5, 6, and 7 are reproduced by permission of the *British Medical Journal*.

silkworm-gut suture is intact, never alters its position however much it may be dragged on.

There are three techniques practised for suprapubic prostatectomy—the Freyer or blind, operation, the Thomson-Walker, or open, operation, and the Harris with its modifications, the plastic operation. In making a comparison of the results of these three techniques we must consider firstly the mortality rate immediate and remote, secondly, the post-operative convalescence, and thirdly, the functional results.

The mortality rate.—The only figures published in this country which give an accurate estimate of the death-rate from prostatectomy are those recorded by Freyer and Thomson-Walker. Freyer records a mortality rate of 5.3% in a personal series of 1,625 cases, while Thomson-Walker states that at St. Peter's Hospital over a period of twenty-nine years there were 2,691 cases with 268 deaths, a mortality rate of 9.9%.

The number of cases quoted by all other observers is so small as to be valueless. Rigid case selection in a series of two to three hundred cases will enable any urologist who is skilled in his craft to produce a mortality rate of less than 5%. Freyer once stated that in one series of 90 cases he did not have a single death, but in the next ten cases there were five. Thomson-Walker in 1920 had a mortality rate of 11.4%, in 1921 1.7%, in 1923 2.1%, and in 1927 9.7%. This experienced urologist states that the fallacy of considering a short period of time and a small number of cases is therefore obvious.

My own figures with the Harris technique are equally variable. In one year, namely 1934, with a comparatively small number of cases, I was on equal terms with those quoted by Harris himself. The following year I had a high mortality rate, due in large measure to inefficient after-treatment. Until I have reached the 500 mark I am not prepared to choose this ground for fighting the battle on behalf of the Harris technique. Rather do I intend to challenge the opponents of the method to prove their case on the questions of post-operative convalescence and the functional results.

As I have stated elsewhere (*Brit. M. J.*, 1936, i, 195) the Harris technique patients now convalesce in comparative comfort unencumbered by large drainage tubes. The latter are the handmaids of sepsis, and by their pressure on surrounding tissues produce infection and sometimes secondary hæmorrhage from the fistulous track.

Those who have been in practice twenty-five years know to their cost how disturbing are the complications of secondary hæmorrhage from the abdominal wall and prolapse of bladder mucous membrane through the suprapubic fistula. If it is necessary to drain the bladder suprapubically with the Harris technique, the smallest-made White's angular tube suffices and its removal need not be delayed after the first week.

The remote mortality rate—that is, six months from the date of operation—is dependent upon the degree of exhaustion produced by the post-operative convalescence and urethral instrumentation. Not one of my patients since 1933 has required the passage of a catheter after the suprapubic wound has healed, except those who have submitted to examination for experimental purposes. As for the nursing of the Harris cases, every Sister who has had experience of the older techniques is loud in her praise of its advantages to patient and nurse alike. Here let me quote a statement made to me by the male nurse at Whipps Cross Hospital, a very experienced and intelligent man who has worked in the genito-urinary ward for eighteen years and has seen the results of three techniques.

Old methods.—"A good deal of hæmorrhage with clots, &c., necessitating cleaning-up and disturbing the patient, apart from ordinary nursing. The treatment-disturbance for the

first three or four days after operation, sometimes longer, is bad for the patient's morale and tends towards depression and unwillingness to put up a good fight for recovery. The use of the Irving's box is not appreciated by the patient, who is only too glad to have it discarded as early as possible, even at the expense of a wet bed."

Of course the suction method of drainage overcomes to a certain extent this disability.

New method.—"Very little hæmorrhage and only in odd cases a few small clots—urine normal in colour and appearance after about three days, which cheers up the patient and as he notices this improvement so do his spirits rise. In straightforward cases the patients pass urine after the urethral tube is discarded on the tenth day and are then able to get out of bed, which reduces the time spent in bed by more than half of the old method."

This reduction in the time of post-operative convalescence, and I reckon that it is at least a fortnight, is one of the greatest advances in treatment, and has an important bearing on the remote mortality rate. The latter seems to be ignored by most urologists.

Simple and I have shown, by a series of cysto-urethroscopic examinations, that healing in the prostatic bed is extremely slow, and long after the suprapubic wound has healed and the patient has returned home, there may remain some raw surface uncovered by mucous membrane in the region where the prostate was removed. In the case of the Harris technique, at least six weeks elapse before healing is complete. What must it be in the older techniques in which no attempt is made to cover the walls of the prostatic cavity with mucous membrane? In those cases in which, on account of the small size of the prostatic cavity, it is a simple matter to cover the whole of the raw surface with mucous membrane, the danger of secondary hæmorrhage is reduced to a minimum.

One of the most noteworthy differences between the post-operative convalescence of the new and the old techniques is the decrease in this troublesome complication. Another important advantage is that once the rubber catheter has been removed—between the tenth and the twelfth days—urethral instrumentation is no longer required, in fact the patient is permanently weaned of all catheters and bougies. Until the adoption of this plastic operation the urologist experienced in all techniques will confess there was always fear that difficulty might be encountered when catheterization or cystoscopy was needed.

During the past three years as many as 30 cases of post-prostatectomy obstruction were admitted to the wards of St. Peter's Hospital. Such a toll of failures is a serious indictment of the operation of prostatectomy. Not only is it disastrous to the morale of the patient to find that the very disability, namely difficulty in micturition, for which he has submitted to operation, has recurred, but also his confidence in his medical advisers is completely undermined.

I have met with two tragic cases of this kind in private practice during the past twelve months, in both of which the prostatectomy had been performed by urologists of experience. The explanation of the cause of the return of obstructive symptoms is quite simple. After the adenomatous mass has been enucleated there is a failure of the trigonal flap and the torn edges of the mucous membrane surrounding the entrance of the prostatic cavity to adhere to the raw surfaces beneath them. The result is that a permanent space is created between the new internal meatus and the triangular ligament.

It is a fluke whether the catheter will pass through the internal meatus into the bladder. More frequently the tip of it is guided behind the trigonal flap. Often the surgeon thinks the catheter is in the bladder, for a drachm or two of purulent urine escapes from its distal end. Owing to the formation of this deformity, difficulty and frequency of micturition persist. These symptoms may not manifest themselves for six months after the operation. Still more serious is the presence of chronic

sepsis. There is no danger whatever of post-prostatic obstruction occurring with the Harris technique. The trigonal flap and the torn edges of mucous membrane are stitched firmly to the raw surfaces beneath. It is this reconstruction of damaged tissues which is the key to our success.

A. W. Badenoch in 1936 examined over 50 cases of mine operated on at St. Peter's Hospital during the years 1934 and 1935. In only one case was there more than one ounce of residual urine and that was in a patient suffering from atony of the bladder, on whom I had operated for a fibrous prostate. Catheterization was a simple matter in all these cases. Frequency of micturition was absent in all cases.

A further series of 50 cases from my private practice gave similar satisfactory functional results, but in none of these was the residual urine tested. At Whipps Cross Hospital there have been 30 cases, dating back to 1934, with excellent functional results. So small a number of cases would be of no value in our estimate of the functional results had we not Harris's testimony from a series of 341 cases, making with mine a total of nearly 500, that not a single patient suffered subsequently from symptoms of obstruction.

To summarize the results of the most modern technique for prostatectomy, reactionary hæmorrhage has been conquered, and the dangers of complications due to sepsis reduced. Absence of a suprapubic fistula has shortened the period of post-operative convalescence for at least a fortnight. The patient is no longer put to the discomfort of wet dressings and wet beds.

Finally the economic advantages to the community of the reduction in the cost of the illness and the time of the patient's inactivity are too obvious to need emphasis.

REFERENCES

- MORSON, CLIFFORD, and SEMPLÉ, J. E., *Brit. J. Urol.*, 1934, 6, No. 3.
MORSON, CLIFFORD, *Brit. M. J.*, 1936 (i), 195.
THOMSON-WALKER, Sir J. W., Lettsomian Lectures, 1930.

Discussion.—MR. WALTER W. GALBRAITH: The results of the Harris operation depend largely on a strict regard to all the points in pre-operative, operative, and post-operative treatment laid down by the late S. Harry Harris.

I had the privilege of seeing Harris on several occasions during his visit to this country in 1935. Three days of that time were spent with me in Glasgow, and I assisted him at an operation. I then, for the first time, appreciated the importance of the careful technique he had developed. He himself took infinite pains and the greatest care with every patient. Harris's technique might be divided into three parts, namely, pre-operative treatment, operation, and post-operative treatment.

(1) *Pre-operative treatment.*—The most strict aseptic precautions with the indwelling catheter; vas ligation before any instrumentation, and a very thorough general examination of the patient, paying special attention to the cardiovascular and renal systems.

(2) *Operation.*—Spinal anaesthesia, or any form of anaesthesia which lowers the blood pressure, is contra-indicated. The ideal anaesthetic is intratracheal gas-oxygen-ether. The technique as described and performed by Harris should be carried out in every detail.

The only modification I have been compelled to make is in the method of closure of the bladder wound. Harris's closure by a double figure-of-eight stitch resulted, in my hands, in a pin-hole sinus through the opening left by the catheter suspension stitch in the centre of the wound. This sinus persisted, in many cases, for about twenty days. Since modifying the technique all the wounds have remained dry after removal of the catheter on the tenth day.

My present method of closing the bladder is by means of a soft catgut stitch uniting the mucous membrane and part of the muscle layer, followed by a second stitch of Lembert type taking a wide bite of the bladder wall, completely covering in the first stitch and ensuring a watertight closure. Both these stitches are stopped one fingerbreadth from the upper margin of the bladder wound. At this site an interrupted catgut stitch of Lembert type is inserted. It takes a wide bite and ensures inversion of the bladder edges. The ends of this stitch are left about three inches long and are fixed to the glass rod supporting the silkworm-

gut catheter sling. The object of this stitch is to permit the raising of the bladder and the easy insertion of a supra-pubic tube, should there be any delayed hæmorrhage with clot retention. I feel that this stitch is of value should clot retention occur, but I have never had to use it.

The size and bore of the indwelling urethral catheter is of the greatest importance when primary closure is desired.

(3) *Post-operative treatment.*—Before the patient leaves the theatre the bladder should be irrigated with a few ounces of antiseptic fluid to make certain that the catheter is clear and all clot expelled. All air must be expelled from the bladder and drainage tubing, the end of which must be kept under fluid. Regular or repeated bladder irrigations are contra-indicated and only if drainage is not free should the catheter be washed through.

Complications.—Blood-clot retention: This is very rare. Harris reported one case of it in his last 273 cases. I, personally, have had none in the last 22 cases (out of 24) in which I performed primary closure.

Urethritis: This should not occur if Harris's pre-operative technique is conscientiously carried out. Should it occur, the catheter must at once be withdrawn, when the urine will leak through the suprapubic wound. It can be collected by means of a suprapubic box.

Peri-vesical sepsis: In my experience this is a rare complication and when it has occurred it has been of slight extent and it has cleared up rapidly.

Contracture of the prostatic urethra or bladder neck: This has not occurred in my series of 53 cases. No instrumentation has been necessary following the operation. All the patients have reported at regular intervals and all have stated that micturition has the calibre and force which they associate with youth.

Mr. C. ALEX. WELLS: I have practised the Harris operation since 1929, and having tried both the vertical and transverse incisions, I am of opinion that the latter gives least trouble in healing, especially in stout patients or in those who develop any degree of intestinal distension after operation. I find Morson's anterior retractor, with speculum blades, of the greatest possible assistance. It enables one to pick up the floor of the cavity under vision. Previously I had found the grasping of the capsule, as described by Harris, far from easy. I think that the postero-lateral hæmostatic sutures are important and should not be omitted. They take up only the edge of the prostatic cavity and exert visible control upon the bleeding. The anterior transverse sutures have given rise to much controversy. I do not like the figure-of-eight stitch advocated by Mr. Morson, but prefer the transverse sutures as described by Harris. I transfix the mucous membrane about $\frac{1}{4}$ in. to either side of the prostatic cavity, but I do not think that my sutures go so deeply as to carry infection into the space outside the bladder; they go widely, but not deeply. This variation in technique possibly accounts for my using rather more of these stitches than Harris advocated.

When operating at a distance from my home I commonly leave a tube in the bladder. This tube is a 26 De Pezzer catheter with the expanded end cut off. The bladder is closed round it by interrupted sutures and the tube itself is closed with a spigot. Bladder drainage is by means of the urethral catheter, but bladder lavage is carried out by running-in lotion through the urethral catheter and allowing it to escape by the suprapubic tube. This eliminates the danger of clot retention, the risk of which is further reduced by the use of a citrate solution containing adrenaline. At the end of two, three, or four days the suprapubic tube is removed and healing of the wound is not delayed. I always drain the space of Retzius in addition.

I cannot agree with Mr. Morson that an inclined position with the head of the bed raised lessens the risk of pulmonary embolism.

Mr. ARTHUR JACOBS: With regard to the complications which may follow the Harris technique, I am aware, from my own personal experience and that of others with whom I have discussed this subject, that there may be sequelæ of a grave nature after the procedure.

To anyone accustomed to performing the Thomson-Walker "open" operation, the technique of Harris's method of dealing with the cavity left after the enucleation of the prostate presented no difficulty. It involved the insertion of three additional sutures, the trigonal and the anterior transverse ones. I have used Harris's method on some sixty cases. In most instances I have reserved it for those in which I was doing a one-stage operation.

I have not made a practice of closing the bladder, having in the majority of my cases inserted a small suprapubic tube, which was usually removed on the second or third day.

A number of these cases have caused me considerable anxiety by developing what I believe to have been a pelvic infection. Some time in the second—or even as late as the third—week after operation, following a seemingly smooth convalescence with primary healing of the wound (except of course at the site of drainage), the patient would begin to exhibit a swinging temperature. At about the same time the urine, which before was being voided either entirely, or for the most part, by the urethra, would begin to leak copiously through the previous site of drainage. In most instances these manifestations would disappear after a few days. In some, however, a typical septicæmic condition had to be dealt with.

In one such case, in which the patient died on the twentieth day after operation, post-mortem examination revealed "a small abscess behind the prostatic cavity into which it drained", and numerous pyæmic abscesses in the cortex and medulla of both kidneys. In another case, in which convalescence had been interrupted in this manner, the patient had to be readmitted to hospital three months after the prostatectomy. I evacuated several ounces of pus through an extraperitoneal incision in the left iliac fossa whence it had tracked from the pelvis.

Apart from infection, I have had two cases with severe secondary hæmorrhages. In one, bleeding occurred on the fifth and again on the fifteenth post-operative day. On the second occasion it was so severe that a blood transfusion was necessary. In the other the bleeding occurred on the twelfth day to be followed by another attack six days later.

Infection is, I consider, caused by the trigonal suture. To insert this suture the needle is made to enter behind the inter-ureteric bar and to emerge as far forward as possible in the prostatic cavity. What is the course that is traversed between these two points? I suspect that in many instances the space of Denonvillier is entered and thus infection is produced.

That Harris's operation may result in a shortened and more comfortable convalescence and that there is a low post-operative morbidity rate, I readily acknowledge. It should not be claimed, however, that the adoption of this technique, even with the employment of rigid surgical asepsis and antisepsis in the pre- and post-operative periods, will eliminate the possibility of infection and hæmorrhage from suprapubic prostatectomy.

Mr. MORTON WHITBY said that he had performed only nine operations in accordance with the technique described by him in an article in the *Lancet* 1934 (i), entitled "Complete closure of the bladder," since he had not the advantage of hospital cases, but he was satisfied from these results that the operation was satisfactory, enabling the patient to micturate normally much earlier than after the open operation. He performed his first operation by this method five years ago. All his patients were alive and well except one who died recently from carcinomatosis. This case was operated upon four years ago, having a partial cystectomy carried out at the same time as a prostatectomy. He did not perform the plastic operation of Harris upon these cases, as he feared the possibility of sepsis from the septic prostatic pouch and subsequent post-operative stricture, and he was satisfied that epithelialization could occur without it. However, he did introduce two lateral sutures as suggested by Sir John Thomson-Walker in his original open operation. A postero-lateral suture was sometimes used to assist hæmostasis in bad cases. Glycerin applied to the prostatic bed was found to be an excellent hydroscopic and assisted hæmostasis. He contended that careful pre-operative and post-operative treatment was the most important part of the procedure, in order to prevent the frightening complications of hæmorrhage or sepsis. By means of a two-way catheter and thermo-flask irrigator now made for him by the Medical Supply Company, even the most resistant cases of cystitis, pre-operative or post-operative, would clear up in forty-eight hours, by virtue of a continuous bladder lavage of hot silver nitrate solution, at a rate of flow insufficient to fill the bladder but keeping the bladder base moist. The apparatus would maintain the temperature constant. By increasing the heat and rate of flow, and using a stronger solution even severe cases of hæmorrhage could be controlled. If these precautions were taken, he was convinced that the operation could be made free from complications, as evidenced by his own small experience.

Mr. E. W. RICHES agreed with Mr. Morson about the comfort of the patient in the post-operative period, but thought that this was still greater if a transverse incision was used. The long vertical incision was admirable for purposes of demonstration, but the short

transverse incision was adequate for the proper performance of the operation. When the bladder was closed completely it should be done with two layers of sutures and its security tested by washing through the catheter before the abdominal wall was closed. As the operation took longer than a simple enucleation of the prostate the choice of anæsthetic was important, and he had found that a low spinal followed by gas-and-oxygen and a complete abdominal field block was the most suitable combination for the majority of patients.

Mr. MORSON (in reply) said that apparently Mr. Walter Galbraith had followed out the late Harry Harris's technique in its entirety. He hoped that Mr. Galbraith would be converted to the importance of the modifications which he had introduced. He entirely agreed that spinal anæsthesia was contra-indicated.

Mr. Arthur Jacob appeared to have been singularly unlucky with some of his cases. Such complications as he had mentioned were often due to errors of technique; the clumsy use of the boomerang needle was one of them. Mr. Jacob had stressed the dangers of secondary hæmorrhage and sepsis. He (Mr. Morson) had dealt in full with these complications in his address at Melbourne in 1935. Unfortunately they were associated with any type of operation for prostatic obstruction, but they were less often met with in the Harris technique than in any other surgical procedure.

In answer to a question as to technique: Silk should never be used as a suture material in the urinary tract; it always promoted sepsis.

In reply to a further question as to the proportion of cases in which he (Mr. Morson) carried out the Harris technique: In all cases in which the major operation was indicated and the bladder was large enough to accommodate the special retractors and gave room for the careful manipulation of the boomerang needle.

He had no criticism to offer to Mr. Riches' preference for the transverse incision. In his opinion it was of little importance which incision was adopted.

Mr. Wells was wise, when operating at a distance from his home, to leave in a supra-pubic tube, for under such conditions he could not personally supervise the after-treatment.

[April 23, 1937]

The Treatment of the Bladder in Spinal Injuries in War

By Sir JOHN THOMSON-WALKER, F.R.C.S.

ANYONE who had to deal with large numbers of cases of spinal injury during 1914-18 will agree that the treatment of the bladder in these cases was one of the surgical failures of the War. The probable cause of the failure was that the methods in use in peace time were unsuitable in war, partly because of the surroundings and partly because of the varying ability and the lack of co-ordination of those through whose hands the cases had to pass.

It will be convenient to refer firstly to the changes in the bladder function that follow injuries to the spine, secondly to show whither failure in treatment led, and finally to describe and compare the different methods of treatment available.

VARIATIONS IN THE FUNCTION OF MICTURITION FOLLOWING INJURY TO THE SPINAL CORD

It has long been established that destruction of the supra-lumbar spinal cord at any point is followed immediately by complete retention of urine, and that at a variable time following the injury the lumbar centre recovers its tone and involuntary reflex micturition becomes established (Corner, 1901). In the large number of cases that came under my care these two stages, namely (1) Stage of retention, and (2) stage of periodic reflex micturition, were clearly defined.

The duration of the stage of retention varied in different cases, the shortest I noted being twenty-four hours and the longest eighteen months. The average duration in thirty consecutive cases was fifty-five days. After some days or hours

the urine begins to dribble away, the bladder remaining distended (retention with overflow).

The stage of periodic reflex micturition, active incontinence, or the automatic bladder, commences gradually and there is a transition period during which the bladder is partly distended with urine but periodic contraction of the bladder wall takes place and expels a quantity of urine. The bladder contraction gradually increases in power until the quantity of residual urine left after micturition is small or there is none at all.

In the fully developed stage of periodic reflex micturition the bladder is a purely reflex organ, with a capacity varying from two to twelve or more ounces of urine and involuntary micturition occurs at intervals of a quarter of an hour to two or three hours.

I was early struck by the effect on the bladder function of injuries to the lumbar spine where the lumbar enlargement of the cord and the cauda equina were affected. It had been the clinical teaching before the War that in the human subject destruction of the lumbar centre and of the cauda equina was followed by complete paralysis of the bladder with overflow. Experimental work on dogs by Golz and Ewald (1896), however, had shown that micturition returned after removal of the whole spinal cord, and Müller (1901) confirmed their results. Langley and Anderson (1894) held that this was due to the branching of efferent nerves and Langley (1900) called it an "axon-reflex". An admirable review of the literature is given by Fearnside (1917).

Returning again to the clinical conditions in the human subject I may quote from my description (1917) of the condition I found where the site of injury was at the lumbar or sacral regions.

"In five cases of injury to the lumbar spine two showed symptoms of a partial lesion of the cord. In one of these voluntary micturition was performed and in one of them there was periodic reflex micturition. In three of the cases the symptoms pointed to a complete lesion, and in each of these there was periodic reflex micturition.

"Lesions of the cauda equina were present in fourteen cases examined. The effect of the nerve injury showed remarkable variation. Three cases of partial lesion of the cauda equina passed water voluntarily and normally. Eight cases of partial lesion had periodic reflex micturition following a stage of complete retention.

"Two cases of partial lesion of the cauda equina had complete retention, one for two months and one for eighteen months after the injury. One case had a complete lesion with retention."

There was here clinical evidence that lesions of the lumbar cord and of the cauda equina in the human subject, although prone to variation, followed in most cases the same sequence of events in the act of micturition as those of the supra-lumbar lesions of the cord. They thus fall in line with the experimental work on animals.

URINARY INFECTION

In a recent paper of much interest Mr. Geoffrey Jefferson (1936) was able to say of a series of cases of injury to the spinal cord under his care, that "no patient who might otherwise have recovered has died of urinary infection." To anyone with experience of such cases in the war of 1914-1918 this statement is in striking contrast to the results under war conditions. But even in peace time these cases are subject to serious urinary infection and we may select as an example one of Mr. Geoffrey Jefferson's own cases recorded elsewhere by Mr. Kenneth Watkins (1936). Of case No. 6 in this series Mr. Watkins writes: "This patient developed a serious urinary infection and at one time it appeared likely that he would die of pyelonephritis."

I shall relate my own experience in such cases during the War, and shall refer to others whose experience was similar. My opportunities of observing cases of spinal

injury with bladder involvement in the middle and late stages of their course were exceptional.

At the King George Military Hospital from May 1915 to the end of 1916 I examined 339 cases of spinal injury in which the bladder function was involved, and as I remained on the staff of the hospital till late in 1919 the total number of cases was much greater. The cases arrived at the hospital about fourteen to twenty-one days after the injury, but the interval was less when heavy casualties were being incurred at the front. The stay in hospital was about a month or eight weeks, and when the patients survived that time they were then drafted on to such permanent institutions as the Star and Garter Home.

At the Star and Garter Home there were 65 beds occupied almost exclusively by cases of spinal injury. During the period already noted I examined 111 cases there and these were added to as vacancies occurred; over 90% of all cases arriving at the Star and Garter Home had had serious infection of the urinary tract.

Of the 339 cases at the King George Hospital 160 died from urinary infection, that is a death-rate of 47.2% during the period of six or eight weeks after the first fortnight following the injury. At the Star and Garter 19 out of 111 cases (17.1 per cent.) at a late stage varying from one to three years after the injury, died of urinary infection. In 1919 I estimated that the total death-rate due to urinary sepsis in spinal cases was 80% (Thomson-Walker, 1919), and having watched these cases in the later stages until 1929 I see no reason to reduce the figure. In the figures published for the American Army the figure of 80% is also given. In a valuable paper by Vellacott and Webb-Johnson (1919) these writers state that at Netley Hospital during the last five months of 1917 the mortality in these cases was 65% of the cases admitted.

This was the record of urinary sepsis in spinal injury in the War—a lamentable tale of surgical failure. How was it brought about? The universal treatment of the bladder in such cases was by intermittent passage of the catheter, and it was septic catheterization that led to the mortality already quoted. The passage of the catheter commenced as early as possible and was repeated as regularly and as frequently as circumstances permitted. Between each passage of the catheter the bladder became distended with grossly infected urine and the infection quickly passed to the kidney along the lumen of the ureter and doubtless also along the ureteric lymphatics. It is true that at the end of the War other methods were being used in some of the areas in France. But it was almost certain that at some part of the journey from the front to the base hospital in this country, the case that had started well in such areas was infected by catheter by some well-meaning blunderer.

There is no difficulty in quoting such cases. The following two are typical:—

I.—J. F., aged 33, fell down hold of vessel September 7, 1918. Fracture dislocation of lumbar spine, injury to cord at twelfth dorsal segment. On his arrival at Star and Garter Home February 14, 1919, bladder showed periodic reflex micturition with three ounces of residual urine. Urine alkaline, purulent, with heavy deposit. Right pyelonephritis. Bedsores at sacrum and heels. My note ran as follows: "This patient was treated at the American Hospital, Boulogne, by 'expression' of urine and got on well. Began to pass water automatically seven to ten days after the accident. On hospital-ship doctor passed catheter in spite of papers stating that the patient must not have a catheter passed. This infected bladder and kidney" (February 28, 1919).

The second case was treated by immediate suprapubic cystotomy and the tube removed during transit.

II.—P. B., aged 24, 21st K.R.R. Shrapnel bullet, complete lesion at third lumbar segment. Removal of bullet and suprapubic drainage at C.C.S. twenty-four hours after injury. I noted: "Suprapubic drain connected with tube and kept perfectly dry at C.C.S. After left C.C.S. drain removed and urine allowed to soak. At Boulogne Base Hospital fourteen days and in Base Hospital in England fourteen days tube out and urine soaking. Bedsores

developed. Then tube reinserted and connected up, wound dry, and bedsores healed." Admitted to Star and Garter Home January 16, 1919. Suprapubic drainage: recurring attempts to micturate. Urine acid, almost clear, slight deposit. Fortunately in this case free drainage of the bladder had prevented ascending pyelonephritis, and bedsores were the worst result of the blundering interference.

TREATMENT

Having discussed the failure of treatment of the bladder in spinal injuries during the War, 1914-18, I can pass to examine the various methods of treatment open for choice in the future. Some of these methods were tried during the War but the organization was imperfect and they were not carried out consistently, but were changed according to the whim of the medical officer immediately in charge. The surgical problem was neither difficult nor complicated. During the phase of complete retention, or retention with overflow, the problem was whether the distended bladder should be emptied and if so how, and during the stage of periodic reflex micturition the problem was the method of collection of the urine and the treatment of sepsis if present.

(1) *Non-interference*

It has been a tenet of our surgical creed since any of us can remember, that a bladder distended with urine, owing to obstruction or paralysis, must be emptied by the surgeon at the earliest time possible. So deeply is this belief impressed upon us by teaching, by reading, and from practice, that it comes as a shock to the orthodox surgeon that any doubt as to its soundness should be raised. The spectres that lie behind are the fear that the bladder may rupture from over distension; or, that having been overstretched, or too long stretched, the involuntary muscle may not regain its contractile power when the obstruction is relieved or when the stage of periodic reflex micturition is due to develop.

Other objections that have been raised are that pain may arise from the distension of the bladder in cases of partial severance of the cord, but these cases are few and are controlled by the use of morphia. Further, it has been stated that there is shock from the distension of the bladder but this is not so in the slow distension by urine of a paralysed bladder. Again, the effect on the renal function and the secreting structures of the kidneys must be taken into consideration.

F. A. Beasley (1917) is a strong advocate of non-intervention in cases of paralysed bladder from spinal injury. He recommends that the bladder be allowed to distend without any local interference until overflow takes place and, eventually, periodic reflex micturition develops. He has seen no damage to the bladder or kidneys and states that no rupture of the bladder ever takes place. So far as rupture of the bladder from distension is concerned, either spontaneously or as the result of treatment, this statement is incorrect, for cases are recorded by Hammond, Vellacott, and Webb-Johnson (1919) and others.

I have no experience of this method and, without more definite evidence that it has no deleterious effect on the bladder function or the renal secretion or structure, I do not consider that it is one to recommend for universal adoption. At the same time I do feel that we have made rather too much of a boggy of the distended bladder. We might, I think, make use of this information in considering the time for intervention in other methods of treatment.

(2) *Expression of the Bladder Contents by Pressure and Massage*

As soon as possible after the injury the distended bladder is gently but firmly compressed and massaged through the abdominal wall with the object of expressing its contents and this is repeated every four or six hours. In some cases this is easy and the bladder is emptied or partly emptied, but in others difficulties arise. Connors

and Nash (1934) warn us that the expression must be commenced before distension becomes too marked. When the bladder is greatly distended the method is painful and the patient rebels. In other cases abdominal symptoms appear, tympanitic distension of the abdomen, pain, and vomiting.

Contraction of the bladder sphincter is a difficulty in this method and may defeat the efforts of the surgeon to expel the urine. To overcome this the prostatic area and bladder neck are massaged simultaneously with the abdominal pressure. Morphine is given hypodermically, while heat to the perineum and the lateral position are recommended. Such drugs as apocodeine, pituitrin, and ergotin followed by adrenaline have also been suggested in order to inhibit the bladder sphincter. To these may be added "doryl" (carbaminoyl-choline), a recently introduced drug (Moir, 1937). Sacral anaesthesia by injection through the sacral hiatus has also been tried.

Instillation of local anaesthetics into the prostatic urethra has been used and one surgeon recommends the passage of large metal instruments to stretch and temporarily paralyse the sphincter. It seems almost unnecessary to point out that the instillation of anaesthetic fluids into the prostatic urethra and the passage of metal instruments is as dangerous from the point of view of sepsis as is the passage of catheters.

It is difficult to obtain statistics of this method. If one can accept the statements of some writers it was the sole method used in their hands, was simple, easy, and successful, and was universally adopted at the end of the War. But these writers only saw a part of the clinical course of the cases which after a few days or a fortnight passed out of their hands. As a result we have little but general statements on which to rely. A few cases of "expression" came under my care in their later stages, but all of these had been spoiled by the passage of the catheter and had become cases of urinary sepsis on catheter life or with late cystotomy. Vellacott and Webb-Johnson recorded 16 cases of treatment by expression in France; of these 10 were sent to England with the bladder in the early or the fully developed stage of periodic reflex micturition. Seven of these had sterile urine and three had mild cystitis. There was a case of rupture of the bladder.

This is a method that requires no instruments or apparatus and it avoids the passage of a septic catheter. It is said to be quite simple and easy. All these facts are strongly in its favour. But there are without doubt certain difficulties and dangers. There is the group of cases, how large I do not know, in which contraction of the sphincter gives rise to trouble and quite a crop of remedies have sprung up to overcome this, not always apparently with complete success. Undoubtedly also, regularity of attention and some skill in manipulation are essential.

It has been said that the continued distension of the bladder with the increased pressure during massage may rupture the bladder, or that it may cause delay in the development of the stage of periodic reflex micturition or even prevent it. I heard a good deal about rupturing the bladder in such cases during the War, but I was never able to get definite figures, so that it is difficult to say how many reports may have arisen from a few cases. That there is a danger of this complication in dealing with large numbers of varying cases by large numbers of medical officers and orderlies of unequal technical skill there can be no possible doubt, and this must be counted as one of the points in disfavour of this method. The valuable figures given by Vellacott and Webb-Johnson prove conclusively that the method does not prevent the development of periodic reflex micturition and this has been my own experience of the revival of the bladder muscle after long distension.

The method is entirely unsuited for cases where serious urinary sepsis has become established. Apart from the fact that the danger of rupture of the wall is greater in an inflamed bladder, massage of a distended infected bladder undoubtedly leads to regurgitation of septic urine along the lumen of the ureter, to the renal pelvis. Regurgitation of urine into the ureter is not difficult to produce as experience with

cystography has shown us in cases where there is no interference with the nerve supply of the bladder. It occurs especially in the inflamed bladder and has been the subject of a number of articles (Pasteau 1914, Kretschmer 1918, Bumpus 1924, Lepoutre 1925, Praetorius 1925). It is certain to occur in cases of nerve paralysis and over-distension of the bladder under the hand of the masseur. There is an excellent example of regurgitation in one of the X-ray illustrations in a recent article on spinal injuries (Watkins, 1936).

(3) *Intermittent Catheterization*

This was the method generally used in the late War and urinary sepsis resulted from its use with a very high mortality.

(4) *The Indwelling or "Tied-in" Catheter*

A condé silk wove catheter is passed at the earliest time possible after the injury, fixed in position and led into a bottle. Washing of the bladder with suitable antiseptics is carried out daily. The catheter is changed twice a week. When the stage of periodic reflex micturition develops the catheter is removed. Time and care must be spent in tying in the catheter and in changing it, and supervision is needed during the passage down the line. If the catheter slips, as not infrequently happens, the bladder becomes distended, and intermittent catheterization is substituted by the attendant. This method, if used as a continuous drain, has the great advantage over intermittent catheterization that it prevents the recurring distension of the bladder and forcing of the ureter. If used with a stopper or clip to evacuate the contents of the bladder at convenient times, it is merely a variant of intermittent catheterization with all its dangers.

In continuous catheter drainage cystitis will probably develop, but there is a free exit and no distension of the bladder, so that the infection does not ascend to the kidney and should be easily overcome when the patient has settled in permanent quarters. Patients vary greatly in the toleration of the urethra to an indwelling catheter and the constant supervision that is necessary to prevent urethritis in peace-time is doubly necessary under war conditions, where the infection is likely to be virulent. Unfortunately a late complication may develop in cases treated by this method where these conditions have not been strictly observed. After the method had been used for a time several cases arrived at the Star and Garter Home, in which a part of the urethral floor and the overlying structures had sloughed at the penoscrotal junction, leaving a gap of $1\frac{1}{2}$ in. or 2 in., as a result of the combined urethritis and the pressure of the tied-in catheter.

These patients were difficult to keep dry, for having reached the stage of periodic reflex micturition the urine was discharged at intervals through the hiatus in the urethral floor. The conventional urine bottle was useless and nothing that did not enclose the penis and scrotum as well would prevent flooding. A retained catheter buckled and projected from the gap. Fortunately plastic operations for the repair of the urethral gap proved successful, the urethral and penoscrotal tissues healing readily so long as the urine was efficiently drained by suprapubic cystotomy during the healing of the plastic operation wound.

(5) *Early or "Prophylactic" Cystotomy*

Early in 1917 I published the heavy mortality that I have given in this article and made a plea for the entire avoidance of the catheter, and the drainage of the bladder by suprapubic cystotomy before any catheter had been passed. I did not expect to avoid cystitis entirely. What I was anxious to avoid was the distension of the bladder with septic urine in the intervals between catheterization, which caused ascending pyelonephritis. Cystitis alone could be cured but pyelonephritis was fatal.

The method I described could be rapidly performed and could, in peace-time practice, ensure a dry patient. From the first the method was persistently confused with the suprapubic drainage of a septic bladder with pyelonephritis, an entirely different procedure. Apart from this, criticism of the method was not wanting. It was said that the surgeons at the front were not sufficiently trained to carry out this method and it should not have been recommended on this account (F. Kidd).

Captain A. J. Hutton (1919) seldom saw a case reach the base "dry" with any method of suprapubic drainage, while he had frequently seen very foul bladders with widespread infection of the space of Retzius. This seems rather a devastating criticism of his fellow-surgeons, and he omits any reference to pyelonephritis, the really important matter. Lieutenant-Colonel Forbes Fraser (1919) stated that the method was largely practised and was the routine method in the second and fifth armies during six months of heavy fighting, catheterization being strictly forbidden, but it was abandoned "on the introduction of the simple and satisfactory method of emptying the bladder by expression." I was unfortunate in meeting with few of these early cystotomy cases. But the small number that came my way were entirely satisfactory.

I had lectured to the medical officers of the Canadian Army on the subject, and was gratified to see two cases treated by immediate suprapubic cystotomy in a Canadian C.C.S. There had been no leakage alongside the tube; mild cystitis easily cleared up, leaving sterile urine, and there was no pyelonephritis. A full periodic reflex micturition developed and the suprapubic fistula healed.

The objections to early cystotomy may be summarized as follows:—

- (1) It is difficult to get a watertight drainage.
- (2) Cystitis is certain to develop and bladder-washing is required.
- (3) "Drainage of the bladder for any long period practically means the abandonment of any attempt to establish automatic function", and "the bladder may be permanently damaged by the adoption of this course".

If these criticisms are reliable, it looks as if early cystotomy were condemned out of hand. But do they really carry much weight? Is it impossible for a surgeon of even moderate ability to produce a watertight suprapubic drainage? I should not have thought so. There is however a method of cystotomy introduced by Mothersill and Clifford Morson (1921) which is even simpler and, slightly modified, would be suitable for these cases. A large rubber self-retaining catheter stretched on a stilet is held ready. The skin immediately above the pubic symphysis is punctured with a scalpel and a large-sized trocar and cannula is plunged directly backwards into the distended bladder. The trocar is withdrawn and the left forefinger prevents the escape of urine. The stretched self-retaining catheter is passed along the lumen of the cannula and the cannula is slipped out, while at the same time the self-retaining catheter is released and expands so as to fit the puncture in the bladder wall. The catheter is gently withdrawn until the mushroom end impinges on the inner opening of the puncture wound. A stitch may be passed through the skin to steady the catheter if the patient is to be moved. For dressing, a small piece of gauze, held by strapping, is all that is required. The catheter leads to a urine bottle and is changed in a week or ten days by stretching it on the stilet, and another is introduced. Washing will keep the bladder clean, but if there is difficulty about this it may be postponed till the base hospital is reached where it can be carried out under surgical conditions. Care in keeping the end of the catheter or extension tube protected, and in the urine bottle, is an obvious necessity. I have already referred to the fact that cystitis without intravesical pressure is not dangerous.

And now in regard to the question of drainage of the bladder preventing the development of periodic reflex micturition. One would have expected to hear this objection used against over-distension rather than against drainage. So far as drainage is concerned, the statement is quite erroneous. The development of the

automatic bladder will take place however long the bladder is drained. The suprapubic fistula at this stage heals without difficulty when the tube is removed.

REFERENCES

- BESLEY, F. A. (1917), *J. A. M. A.*, **69**, 638.
 BUMPUS, H. C., Jr. (1924), *Tr. Am. A. Genito-Urin. Surg.*, **17**, 17.
 CONNORS, J. F., and NASH, J. E. (1934), *Am. J. Surg.*, **26**, 159.
 CORNER, E. M. (1901), *Ann. Surg.*, **2**, 457.
 FEARNSIDES, E. G. (1917), *Brain*, **40**, 149.
 FRASER, FORBES (1919), *Brit. M. J.* (i), 293.
 GOLZ, FR., u. EWALD, J. R. (1896), *Arch. f. d. ges. Physiol.*, **63**, 362.
 HAMMOND, T. E. (1926), *Proc. Roy. Soc. Med.*, **19** (Sect. Urol., 12).
 HUTTON, A. J. (1919), "Manual of War Surgery", S. Barling and J. T. Morrison (Eds)
 JEFFERSON, GEOFFREY (1936), *Brit. M. J.* (ii), 1125.
 KIDD, F. (1919), *Brit. M. J.* (i), 399.
 KRETSCHMER, H. (1918), *J. A. M. A.*, **71**, 1355.
 LANGLEY, J. N. (1900), *J. Physiol.*, **25**, 364.
 LANGLEY, J. N., and ANDERSON, H. K. (1894), *J. Physiol.*, **10**, 410.
 LEPOUTRE, C. (1925), *Arch. d. mal. d. reins*, **2**, 146.
 MOTHERSILL, G. S., and MORSON, CLIFFORD (1921), *Brit. M. J.* (i), 418.
 MOIR, CHASSAR (1937), *Lancet* (i), 261, 263.
 MÜLLER, L. R. (1901), *Ztschr. f. Nervenheilkunde*, **21**, 86.
 PASTEAU, O. (1914), *J. d'uro.*, **6**, 17.
 PRAETORIUS, G. (1925), *Ztschr. f. Urol.*, **19**, 743.
 THOMSON-WALKER, J. (1917), *Lancet* (i), 173.
 Id. (1919), *Brit. M. J.* (i), 325.
 VELLACOTT, P. N., and WEBB-JOHNSON, A. E. (1919), *Lancet* (i), 733.
 WATKINS, K. H. (1936), *Brit. J. Surg.*, **23**, 734.

Mr. KENNETH WATKINS, discussing the behaviour of the bladder in complete lesions of the conus medullaris and cauda equina, pointed out how such patients urinated by straining with their abdominal muscles and in this way expelled the urine retained within the bladder. He showed that although the detrusor muscle and internal sphincter were not entirely paralysed they were very ineffective in expelling urine from the bladder. There seemed to be a mechanical resistance to emptying of the bladder in the region of the triangular ligament. If the patient urinated regularly by straining with his abdominal muscles he could keep himself fairly dry, but incontinence was always present in some degree, especially at night-time. On the other hand, transverse lesions of the spinal cord at a level above the sacral segments resulted in an entirely different type of bladder function. At frequent intervals powerful contractions of the bladder wall occurred and emptied the bladder, a true reflex micturition which differed from the normal only in that the patient was quite unable to control it. This could be described as periodic reflex micturition. It was a much more perfect bladder function than the first type, but much less satisfactory from the patient's standpoint.

With regard to infection, he thought that the second type of case—that of a transverse lesion, with an active reflex micturition, was much more liable to serious infection of the upper urinary tract. In his experience the less active bladder, from lesions of the conus or of the cauda equina, had not caused upper-tract infection of any severity. Non-instrumentation and expression of the bladder for the initial stage of acute retention had been undertaken in several cases, occasionally with great success. In two cases, however, a single unauthorized catheterization in the early stages of this treatment had led to very severe cystitis and a slough of the whole lining of the bladder wall, necessitating suprapubic drainage. Probably in cases with transverse cord lesions and true periodic reflex micturition there would be ready healing of a suprapubic cystostomy sinus, but the conus and cauda equina lesions, with the less active bladder and a large amount of residual urine, might prove more resistant. One case with an incomplete cauda equina lesion had shown fairly rapid healing of the suprapubic cystostomy sinus after re-suturing.

Section of Odontology.

President—W. WARWICK JAMES, O.B.E., F.R.C.S., L.D.S.E.

[March 19, 1937, contd.]

Three Cases of Osteomyelitis.

By H. F. HUMPHREYS, O.B.E., M.C., M.B., M.D.S.

I. Acute Osteomyelitis and Death following Dental Extraction.

The patient, A. S., a small, anæmic, poorly nourished man, aged 33, reported at the Birmingham Dental Hospital on March 9, 1936, with a history of extraction of the right 2nd lower molar about a week previously, under local anaesthesia, followed by swelling over the tooth socket which had rapidly spread round the jaw to the left side.

There was considerable swelling over the mandible on both sides, with marked fluctuation, and quantities of pus oozed from round the lower premolars and first molars, which were very loose. The site of the previous extraction appeared to be quite healthy. Temperature 103° F.

Three loose teeth were extracted on either side to allow drainage, and the patient was admitted to the General Hospital. Following extraction the condition improved for a week, the temperature varying from normal to 100° F.

March 20 : The temperature again rose and cellulitis of the face developed. Anti-streptococcal serum was given, and repeated on the 22nd.

March 25 : An incision was made over the left parotid region and large quantities of pus were freed. Four counter-incisions were made for drainage.

March 26, 30 : Two blood transfusions were given.

March 31 : Respiration, which had remained constant at about 25, suddenly rose, other signs of septic pneumonia developed, and the patient died on April 1.

Post-mortem examination showed suppurating bronchopneumonia involving the whole of the left lung and lower lobe of the right, empyema of the left pleura, and cavernous sinus thrombosis.

No bacterial culture of the pus was taken, as the infection was clearly a mixed one, and it is plain from the progress of the case that the "soil" was here more important than the "seed", the fatal termination being due to abnormally low resistance. It is possible, however, that in this case outside infection was introduced at the time of the local injection or the extraction.

II. Subacute Osteomyelitis of the Mandible.

The patient, A. N., a rather poorly nourished boy aged 12, had the right first lower molar extracted at the Birmingham Dental Hospital, without difficulty, under gas anaesthesia, on February 29, 1936. Three weeks later he returned with a brawny

swelling over the angle of the jaw and discharge of thick pus from the socket. Temperature 100° F.

Skiagrams revealed a sequestrum lying in the socket. I removed this without difficulty, but the swelling did not subside. The socket healed, the boy's general condition improved, the temperature became normal and he returned to school, but a sinus remained, discharging pus. Skiagrams showed normal appearance of the bone surrounding the second molar and the unerupted third molar.

The radiographic appearance of the ascending ramus, though suspicious, did not, in my view, warrant interference, in view of the boy's good general condition, and I waited for local signs of sequestrum formation. The condition remained unchanged until September, when the swelling over the mandible appeared to be spreading upwards towards the sigmoid notch. Fearing involvement of the joint I transferred the case to Mr. Mills at the General Hospital. The appearance in the skiagram at this stage suggested a patch of necrosis in the ascending ramus.



A. N. (Case II) September 1936.

Operation, 23.9.36 (Mr. Mills): An incision was made along the posterior border and angle of the mandible, the soft tissues were turned forward and the ascending ramus was exposed. There was no visible pus and the gouge went into the bone in the area indicated by the dark shadow in the skiagram. A small piece of dead bone, about $\frac{1}{4}$ in. in diameter, was removed. Healing was uneventful and the sinus in the mouth closed.

Three months later the boy returned to the Dental Hospital with some local soreness in the mouth at the site of the old extraction. A piece of bare bone was sticking through the gum, and I removed a loose sequestrum about $1\frac{1}{2}$ in. long, $\frac{1}{4}$ in. deep, and $\frac{1}{8}$ in. thick, from the outer alveolus, extending from the second molar to the second premolar. Healing, both inside and outside the mouth, is now complete.

The curious feature of this case is the spread of infection from the original site to the middle of the ascending ramus, with little involvement of the intervening bone surrounding the second and third molars.

III. Chronic Osteomyelitis of the Superior Maxilla.

The patient, M. S., a woman aged 48, reported at the Birmingham Dental Hospital early in February, 1935, with a swelling over the left upper jaw. The history is as follows:—

She had been edentulous (except for six lower front teeth) for twenty years and had worn a denture. Six months previously the upper denture had caused soreness

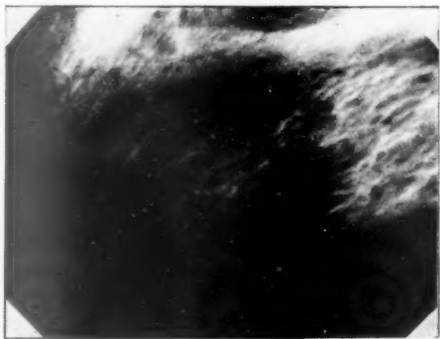
followed by swelling on the left side and use of the denture had been discontinued, but the swelling persisted though without very much pain. The patient's general condition was fairly good.

Examination showed a soft boggy swelling over the left side, extending into the cheek and palate, and pus discharging through several sinuses; examination with a probe revealed bare bone.

Skiagrams showed a condition of caries of the bone with the cancellous spaces very much enlarged, and separated only by thin trabeculae.

Bacteriological examination of the pus revealed no specific flora showing, only mixed pyogenic organisms. The Wassermann reaction tested at Selly Oak Hospital was negative.

On February 12, 1935, at the Birmingham Dental Hospital I opened up the area of the swelling and removed large quantities of necrosed and carious bone which reached from the tuberosity to the canine region. Having removed this to a depth of about half an inch I still found myself dealing with somewhat soft bone and stopped for fear of entering the antrum. Subsequent examination of the antrum by Mr. Strong showed that cavity had not been opened. Following operation the swelling



M. S. (Case III) February 12, 1935.

subsided, all superficial inflammation disappeared, and one sinus remained with bare bone palpable at the bottom.

Since then the patient has been well, and generally speaking comfortable, except that she cannot wear the upper denture. On three or four occasions during the past two years she has suffered recrudescence of pain and on each occasion skiagrams have shown one or two sequestra, which I have removed under local anaesthesia. She was last seen on March 9 this year. There is one small sinus apparently dry and the patient is quite comfortable.

This case very closely resembles that shown by Mr. G. T. Hankey in March last year.¹ The sole cause, as far as can be ascertained, is traumatic ulcer. The bone lesion in the early stages resembled caries rather than necrosis as there was no definite line of demarcation between the healthy and diseased bone. In the later stages both the skiagrams and the clinical features show a closer approximation to true necrosis, with the formation of sequestra. If this tendency increases complete healing may ultimately result but the condition may, as in Mr. Hankey's case, be slowly progressive.

¹ *Proceedings*, 1936, 29, 1099 (Sect. Odont., 41).

[March 20, 1937]

Two Cases of Osteomyelitis of Mandible.—GEORGE T. HANKEY, L.R.C.P., M.R.C.S., L.D.S.E.

I.—G. J., female, aged 29.

Family history.—Not relevant.

Personal history.—Good health. No previous illnesses.

On examination.—The patient now demonstrates the final stage or cure of an acute osteomyelitis of the mandible. She was shown at the clinical meeting on March 23, 1936 (see *Proceedings*, 29, 1102, Sect. Odont., 44). The whole of the left



Case I.—Cure. New bone has bridged across the gap from $\bar{1}3$ to the left condyle. Function and occlusion good.

body posterior to $\bar{1}3$, and the ascending ramus, with the coronoid process were removed as sequestra; in addition, portions of the lower border were removed as far round on the right side as $\bar{6}$. The jaw was kept in correct position during sequestration by the splints still being worn: the mandible was banded to the upper jaw for twelve months. New bone has now bridged across the gap from $\bar{1}3$ to the condyle, and the jaw is functional and in correct occlusion. (See skiagram.)

II.—Patient, male, aged 46.

April 1934: Ulceration and infection of $\bar{8}$ gum-flap, followed by acute osteomyelitis of right body and ascending ramus of mandible. Patient critically ill. Large external incisions for drainage, removal of sequestra. Eventually right body with $\bar{8}765$ removed; also ascending ramus and coronoid process (see figs. 1 and 2).

C.P.,

f an
g on
left



FIG. 1.—Case II. Complete sequestration of right body of mandible posterior to 4 | and of ascending ramus with coronoid process. (Antero-posterior view.)



FIG. 2.—Case II (as fig. 1). (Lateral view.)

oved
ound
tion
elve
and

steo-
r ill.
body
1 2).



FIG. 3.—Case II. New bone formation has bridged across the gap from the condyle to 4|. Jaw now normal in occlusion and function. (Lateral view.)

June 1934: Metal cap splints fitted to upper jaw and remaining lower teeth. Lower jaw banded to upper in correct occlusion for nine months.

July 7, 1935: (Fig. 3.) New bone has bridged across the gap from the right condyle to 4|; the jaw is now functional and in correct occlusion.

EIGHT CASES SHOWN BY WARWICK JAMES,
O.B.E., F.R.C.S., L.D.S.E., (President):—

I.—Multilocular Cyst.

J. D. H., male, aged 54.

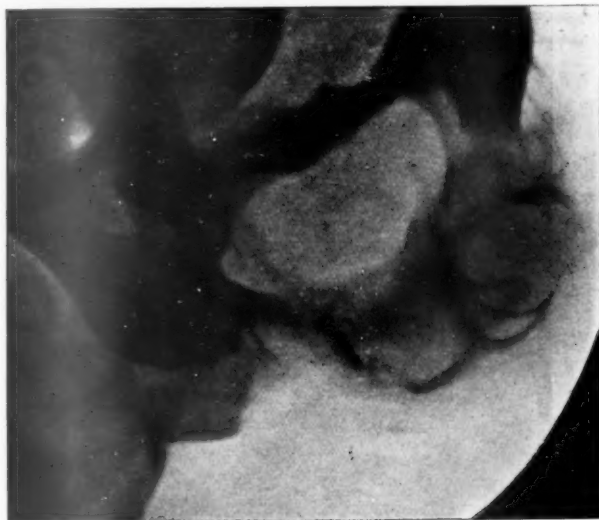
History.—Swelling in right mandible, first noticed inside mouth three and a half years previously, has been gradually increasing in size. Patient unable to wear denture after six months. No pain, discomfort, discharge, or swelling elsewhere. Edentulous since 1919.

Condition (January 1937).—Size and appearance of swelling shown in photograph, and casts of face and jaws. On examination: A large, fluctuating, rounded swelling in the right mandible bulged upwards into the mouth and outwards on the lateral aspect of the mandible, causing an unusually large protuberance. Fluctuation could be obtained through the whole of this area. The inner alveolar border was intact, but the lower border of the mandible was irregular and could be felt to be considerably everted (well shown in the X-ray films). The area involved extended from the region of 3| to beyond 8|. The multilocular character is obvious in the distorted lower border of the mandible.

Operation (January 1937).—The fluid contents were aspirated with a large needle, another needle being introduced to allow air to enter; about 70 c.c. were removed. No cholesterol crystals were seen in the fluid that escaped or during the operation. Buccal and lingual incisions were made from the ascending ramus almost to the mid-line. The tissue included was removed, with almost the whole of the lining

of the large loculus which, from this aspect, clinically resembled a dental cyst. The lining of the remaining loculi was removed as thoroughly as possible. A fragment of bone was taken from the buccal aspect for microscopical examination, and a thin layer was broken and turned upward. Hæmorrhage was free and the cavity was packed with paraffin and flavine. Some hæmorrhage occurred after the patient returned to bed and packing was necessary. There was anaesthesia of the right lip.

Complete removal of the lower border of the mandible was desirable but could not be effected, as fracture and collapse of the bone would almost certainly have



CASE I.—Multilocular cyst.

occurred. The patient has been told that a second operation will most probably be necessary. So far he has made an uninterrupted recovery.

Microscopical section.—(Small fragments only have been examined so far.) The sections show strands of epithelium intercommunicating, and large areas undergoing degeneration.

Contents of cyst.—Report received from Courtauld Institute of Bio-Chemistry :—
Non-protein nitrogen : 24 mgm. % ; total protein : 4.07 gm. % ; urea : 30 mgm. % ;
cholesterol : 147 mgm. % ; bile-pigments : Fouchet's reaction positive.

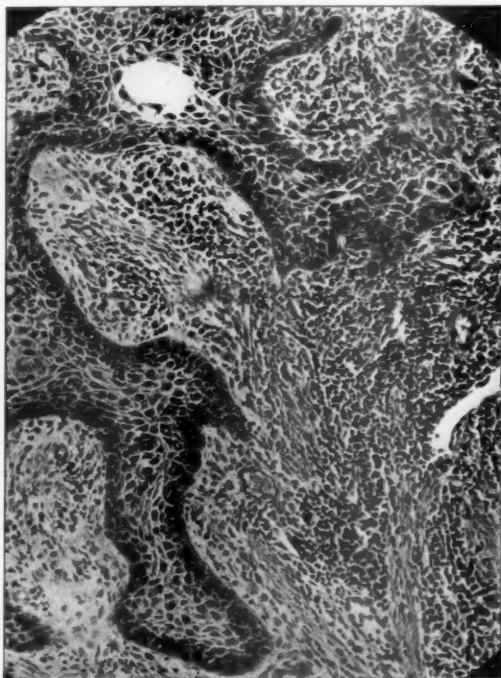
II.—Squamous-celled Carcinoma.

F. W. F., male, aged 60 (aged 50 at operation).

In November 1927 the patient presented a large sloughing ulcer on the alveolar ridge of the mandible, extending from $\overline{6}$ to $\overline{3}$. The ulcer had everted edges but was not hard. There was no fixation of the tongue, nor were glands evident. There was a little thickening into the floor of the mouth on the left side. The patient had only noticed the condition for ten weeks. A section made for diagnostic purposes at the

Royal Dental Hospital was reported upon as epithelioma (*see figure*). Further sections made at the Middlesex Hospital (Pathological Department and Dental Research Department) confirmed this diagnosis. The Wassermann reaction was negative.

Operation (Mr. Turner Warwick and Mr. Warwick James).—A vertical incision, 4 in. in length, through mid-line of the lip, and two horizontal incisions at right-angles to the lower end in the submental region. The tissues were reflected and bone



CASE II.—Squamous-celled carcinoma.

was excised from 6 to 3 but a thin layer of the lower border of the mandible was left intact. Careful dissection of the parts was carried out, including the glands; the flaps were sutured and the wound was packed. Considerable hæmorrhage occurred ten days after the operation. The patient was very ill for a period and made a slow but good recovery. A denture was made. Later the mandible fractured. Consolidation followed with some deformity. An expansion plate was introduced to correct the occlusion. The present position was obtained and a denture—which is still being worn—was put in.

III.—Extensive Osteomyelitis of the Mandible.

J. A., male, aged 62.

History.—June 1930: Teeth extracted.

January 1931: Patient began to wear dentures but at the end of the month he had pain and a swelling beneath the chin rapidly increasing in size.

February 1931: Admitted to Middlesex Hospital under Mr. Pearce Gould, having a red tawny swelling beneath the chin, extending backwards on both sides into the submaxillary regions and upwards over the ramus of the mandible. There was œdema and great tenderness, but no area of fluctuation. Fluctuation developed beneath the chin.

Two operations were performed: (1) A large quantity of pus was evacuated and a drainage tube inserted in a cavity reaching far back on the right side. The pus contained streptococcus. (2) A similar abscess developed on the left side about a week later and was treated in the same manner.

March 1931: Transferred to the Dental Department, when the following condition was found: Loss of definition along the lower margin of the mandible, necrosed bone in the mouth, and sinuses beneath the chin and the body of the mandible on the right and left side.

Operation (April 1931).—The large scar adherent to the mandible beneath the chin was excised, necrosed bone removed, and the mandible tunnelled almost to the angle on the left side and about two-thirds of the distance on the right side. Drainage tubes were inserted. (The procedure decided upon depended upon the conclusion that the central artery had been destroyed, and that although the periosteal vascular supply was exceedingly good, as was demonstrated by the amount of new bone formation, the central area appeared unable to recover on account of the infected condition. The procedure appears to be justified by the result obtained.) The bacteriological report states that streptococci and diphtheroids were present.

In November 1932, and in February 1933, localized swellings occurred, incisions were made, and small fragments of necrosed bone were removed.

In April 1933 the patient was wearing dentures and had completely recovered.

IV.—Papilloma of the Palate.

S. S., male, aged 59.

History.—A small swelling had been present for some years. Small pieces used to break off and sometimes this breaking-off was effected with the tongue. In May 1930, when seen as an out-patient, there was no evidence of a papilloma. The remaining teeth were extracted. In April 1936 the patient was admitted to hospital.

Operation (April 1936).—Crescentic incisions enclosing the growth were made through the whole thickness of the mucoperiosteum. The mass was removed intact by a gouge cutting away the area of bone immediately beneath. The bone was apparently not involved and the wound was stitched.

Microscopical sections.—Report: Squamous-celled papilloma; non-malignant.

V.—Fibrous Epulis between 2 & 1].

C. H., male, aged 17.

Patient presented a firm swelling on the labial and palatal aspect, with a communication between 2 & 1]. There was a small slough where 2] impinged. The outer part was somewhat smaller, redder, and more granular. X-ray films showed no bone destruction.

Operation.—Incisions were made through the muco-periosteum, and the two teeth with their bony sockets and the tumour were removed in one piece. The patient made an uninterrupted recovery.

The interest in this case is that the patient has typical formation of the "lips apart" group, with tension ridges and gingivitis. The mouth has been thoroughly "cleaned up"—with marked improvement.

Microscopical sections.—Report: "Showing fibromatous condition."

N.B.—Infection of the mouth is always present in these cases, and the writer believes that the condition is associated with failure to maintain the negative pressure which should be normal to the mouth.

VI.—Dilated Composite Odontome.¹

E. C., male, aged 54.

Patient presented a cavity in the right maxilla, the result of the removal of a molar tooth. Pus was discharging and the crown of another molar could be seen. Several unsuccessful attempts at removal had been made by different operators. There was some bulging of the right maxilla and cheek, and also of the palate. On examination a hard substance could be felt beyond the crown of the tooth, but no margin could be defined. X-ray films showed a large globular opacity.



CASE VI.—Dilated composite odontome.

Operation.—The tumour was removed with some difficulty, a considerable amount of bone having to be cut away. The healing of the wound was uneventful.

Although the specimen was placed in formalin immediately, the surrounding soft tissues had been so destroyed by the suppurative process that they revealed nothing of importance.

Macroscopical examination of the ground section reveals the character of the tumour.

VII.—Dental Cyst (Right Mandible).

M. P., female, aged 41.

History.—In March 1935, patient had noticed a swelling for about two weeks; "thought it was mumps." There was discharge into the mouth and an aching pain kept her awake. X-ray films revealed a very extensive cyst reaching above the coronoid notch of the right mandible, involving a large part of the coronoid process, the ramus, and condyle (fig. 1).

¹Case reported at the F.D.I., Paris, 1931.

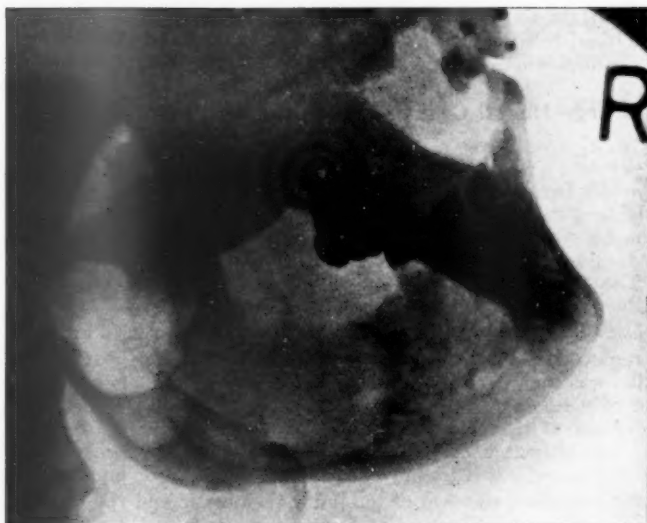


FIG. 1.—CASE VII.

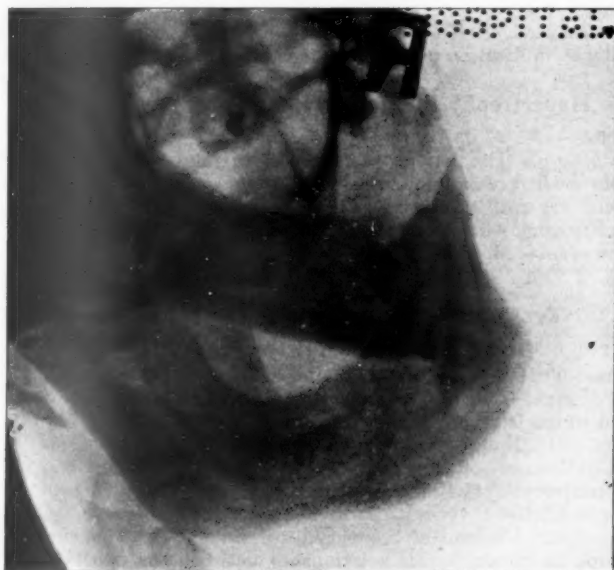


FIG. 2.—CASE VII.

Operation.—The cyst was opened and loose bone removed. The lining was dissected from the bony cavity with ease anteriorly, but with some difficulty in the region of the coronoid and ramus. The cavity has gradually diminished (see fig. 2).

A small cyst in the terminal phalanx of the middle finger was shown by X-ray films. The blood-calcium did not show any abnormal deviation.

Microscopical sections show epithelium usual to a dental cyst.

VIII.—Large Dental Cyst arising in the Left Maxilla and Obstructing the Nose.

R. J. L., male, aged 40.

History.—In October 1936 the patient had complained of discharge from the nose for eighteen months. There was a swelling in the floor of the nose and X-ray films revealed a cyst occupying the whole of the left maxilla, obliterating the antrum and extending across the middle line towards an unerupted canine of the right maxilla. The temporary canine was still present. A sinus existed in the region of 11, but the greater amount of the discharge was from the nose.

Operation.—Incisions were made in the 11|12 region. The foul contents of the cyst were removed, and a large cavity involving the whole of the left and part of the right maxilla was found. Exploration of the cavity with a finger revealed the bone of the floor of the nose on the left side to have been absorbed, although immediately inside the orifice of the nostril new bone had been produced to form a rounded eminence. The patient had not felt well for a year. An abscess had occurred in the region of 11 about ten years previously. The suppuration and the foul condition of the cavity precluded removal of the lining membrane and the unerupted canine, which was not exposed. The patient has made an excellent recovery although still presenting a large cavity which requires attention. The cavity has contracted and a passage through the nose is now so clear that he can breathe freely through it. There is a marked improvement in general health.

Microscopical section.—The surface tissue removed revealed epithelium, detached in places with an infiltration of lymphocytes and plasma cells beneath it.

Fibrous Hypertrophy of Maxilla.—HERBERT GORDON, L.D.S.E.

Miss P., aged 23.

Personal history.—The patient was referred on October 21, 1936, by Dr. Kenneth Harris, whom she had consulted in regard to her general health. She had not noticed any inconvenience until the last two years, but was now experiencing difficulty in speaking and singing. She was extremely nervous.

On examination.—Mouth condition :—

Lower 8 7 6 4		5 6 7 8 Septic roots.		Upper 8 6		Septic roots.
3 2 1 1 2 3 4			Sound teeth.	7 5 4 3 1 1 3 4 5 6 7 8 Sound teeth.		

Posterior to 5|5 the maxilla had hypertrophied to form two masses which nearly met in the mid-line ($\frac{1}{16}$ in. separation), almost filling the palate.

Relation of jaws.—When closed, the upper posteriors came into contact with the roots present in the lower.

Treatment.—(1) Rough impression and skiagrams taken. (2) Scaling and cleaning. (3) Removal of all septic roots in lower jaw (avertin and nitrous oxide). Uneventful recovery. (4) Removal of upper molars and hypertrophic tissue. The operation was hindered very badly by excessive hæmorrhage. Gum flaps were stitched together. Uneventful recovery. (5) Badcock's expansion plate inserted in an attempt to obtain better relationship between the two jaws. (6) Dentures inserted.

Comment.—It was decided to remove all the upper molars, to lessen the possibility of recurrence.

POSTSCRIPT (July 1937).—No recurrence.

Cleft Palate.—E. A. HARDY, L.R.C.P., M.R.C.S., L.D.S.E.

Male adult, shown to illustrate a method of stabilizing a denture by means of a gold jacket crown.



Treatment.—To bring the upper lip forward and evert the vermillion border to a more normal position would tend to unstabilize the denture. By gold-jacket crowning $\bar{3}$, without undercuts, a considerably increased support is given to the denture and there is no likelihood of decay.

Section of Orthopædics

President—B. WHITCHURCH HOWELL, F.R.C.S.

[April 6, 1937]

Fractures of Tibial Tuberosities.—C. E. KINDERSLEY, F.R.C.S.

G. H., aged 41. Estate carpenter.

There are few fractures in which reduction is more difficult than these, and the method which I am about to describe suggests that it may be possible to obtain good reduction without operation in this type of fracture.

There is usually a wide separation of the tuberosity from the shaft, and in some cases both tuberosities may be fractured and the shaft slides up between them. Such fractures should be treated by distraction, disimpaction, and compression, which are carried out as follows:—

A wire is passed through the femur clear of the knee-joint. A second wire is passed through the tibia well below the fracture, the limb is then distracted on a frame with a pull of about 40–50 lb., and mobilization of the fragments is achieved by manual manipulation, but if this cannot be achieved a Steinman's pin is thrust into the fracture line and the fragments disimpacted with it. This allows the distracting force to correct the linear displacement of the fragments.

The next step is circular compression and this is achieved by applying a rubber bandage around the fractured end of the bone in such a manner as to produce sufficient pressure upon the fragments; each successive turn is made tighter than the last until considerable tension has been applied. This force should be practically non-traumatizing, provided the width of the bandage used is adequate, and for this purpose I use a 3 in. plain rubber bandage. Finally, a few blows on the bandage in order to "shake" the fragments, are applied with a heavy mallet. This allows the circular compressive force of the bandage to impact the fracture completely and—if distraction and mobilization have been adequate—the complete reconstruction of the tibial articular surface. The rubber bandage is then removed and the circulation of the limb allowed to re-establish itself, and an unpadded plaster, with wires incorporated in it, is applied from the toes to the groin.

I recently had the opportunity of testing this method in a second case of tuberosity fracture, with lateral displacement of the outer portion of the external tuberosity, the inner portion of the articular surface of this tuberosity being driven down into the substance of the tibia. It was obviously impossible to replace these particular fragments without operation, and having opened the joint and explored the site of fracture, I discovered that the external cartilage was torn and displaced anteriorly. I removed this and elevated the fragments of joint surface into their correct position. I made an attempt to reconstruct the top of the tibia by manual effort but found that I could not apply sufficient force to achieve any adequate result. I then applied a sterile rubber bandage after temporary closure of the wound, and carried out the manœuvres described above. On removal of the bandage and inspection of the site of fracture through the wound, I was able to demonstrate that the whole fracture was in perfect position, even though I had failed to replace



FIG. 1.—Tibial tuberosity fracture; antero-posterior view, showing the widening of the articular surface, shortening, and lateral displacement of the shaft of the tibia.



FIG. 2.—Lateral view, showing shaft of tibia driven up into the head.



FIG. 3.—After reduction. Showing distraction and realignment of the shaft and reconstruction of the articular surface. Suggesting that the cancellous bone has been "pulped", and the inevitable failure of bone pegs or screws to maintain position.



FIG. 4.—After reduction. Showing satisfactory reconstruction and alignment of both bones. This illustrates the "pulping" at the site of fracture.

the tuberosity by manual effort, showing that the amount of force necessary can be applied by a bandage but cannot be applied by hand. A subsequent skiagram showed that the position was maintained, and now—two months after the fracture—it is impossible to see any departure from the normal in a skiagram.

The after-treatment should be to avoid weight-bearing on the tibia until sufficient consolidation has taken place.

The principle of circular compression is no doubt applicable to fractures in other situations, such as the femoral condyles, tarsus, and ankle-joint.

Fractured Os Calcis.—C. E. KINDERSLEY, F.R.C.S.

The difficulties associated with reduction of a fractured os calcis are: (1) That such fractures are almost always impacted, leading to a considerable widening of the bone. (2) Although there is rarely any antero-posterior shortening of the os calcis, even when the fracture extends into the plantar aspect, there is usually some angulation at the site of fracture on this aspect, with the long plantar ligament intact and acting as a hinge. Owing to the presence of the long plantar ligament any force applied in a posterior direction is unlikely to disimpact the fracture, as it will be taken up by the long plantar ligament and very little will be applied to the upper portion of the bone; this is borne out by what has been observed by many, namely that there is a tendency for the anterior portion of the bone to be displaced by such traction.

It was this consideration that led me to devise the following method:—

(1) A Steinman pin is thrust through the junction of the middle and lower thirds of the tibia, parallel to the axis of the knee-joint.

(2) A second Steinman pin is passed through the upper posterior corner of the os calcis.

(3) The limb is now hung in a distraction apparatus with the knee flexed to a right angle, and the fracture distracted by applying a tension of 70–90 lb., which is measured accurately by a spring balance.

(4) At this stage, with the tension still operating, I employ a wide-headed punch to the lower surface of the os calcis at the estimated site of the fracture, and give this two or three hard blows with a heavy mallet in an upward and backward direction. This “shaking force” allows the immediate disimpaction of the fracture by the tension which is operating at the same time, and it will be noticed that when this occurs the balance will show a lower reading, indicating that the points of insertion of the pins have been separated by a measurable distance. The redresseur, such as is used by Bohler, is now applied across the heel and screwed up, in order to reduce the widening of the bone. A very efficient substitute for the redresseur is a Thomas’s wrench. The limb is now encased in an unpadded plaster from the tubercle of the tibia to beyond the toes, with the foot in a position at right angles to the limb, and it is of importance to mould this plaster well under the longitudinal arch of the foot. The pins are incorporated in the plaster.

The fracture of the os calcis having been reduced and any downward pressure on the astragalus removed by means of the pin through the tibia, there is no tendency for the anterior fragment to become redisplaced, for any muscles which exert an action upon it tend to raise rather than depress it. The posterior fragment is maintained in position by the pin through its upper corner and the moulding of the plaster.

A case is shown (W. G., male, aged 50) in which this method has been applied. There is perfect reconstruction of the os calcis and very good function has been obtained, though the subastragaloid joint remains stiff. This particular sequela to os calcis fracture is so constant as to be expected.

I have so far applied this method in two consecutive fracture cases with an almost perfect reposition of the fragments, and suggest its use by other surgeons before its true value can be estimated.



FIG. 1.—Lateral view of os calcis showing flattening of the bone, impaction of the upper portion, and loss of the plantar curve.

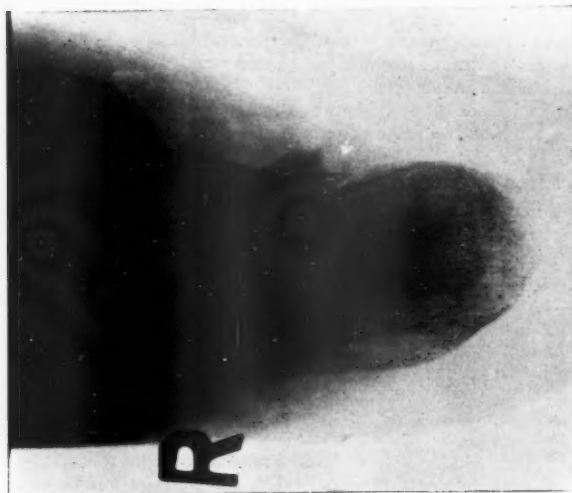


FIG. 2.—Fractured os calcis. Antero-posterior view showing the widening of the bone and impaction of the fragments.

FIG. 2.—Fractured os calcia. Antero-posterior view showing the widening of the bone and impaction of the fragments.

FIG. 1.—Lateral view of os calcis showing flattening of the bone, impaction of the upper portion, and loss of the plantar curve.

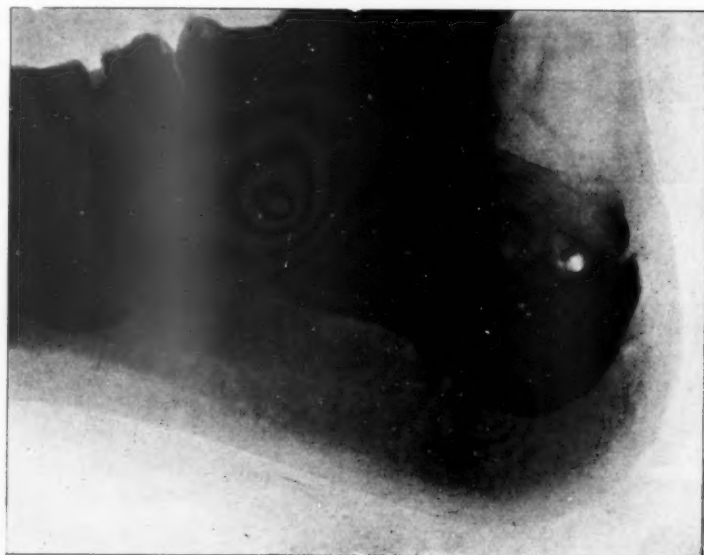


FIG. 3.—After reduction. Satisfactory reconstruction of upper surface and reappearance of the plantar curve.

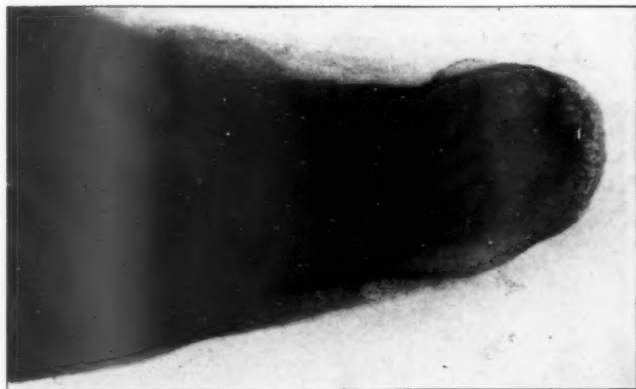


FIG. 4.—After reduction. Antero-posterior view, showing full recovery of length and width.

Reconstruction of Thumb.—C. E. KINDERSLEY, F.R.C.S.

T. H., aged 14 years.

This case is shown to illustrate reconstruction of the thumb, using skin supplied by the radial nerve to cover the palmar surface of the new digit.



FIG. 1.—Healed hand showing scar and base of first metacarpal under the skin.



FIG. 2.—Small piece of bone placed under skin on dorsum of hand.



FIG. 3.—Pilot thumb elevated and raw area covered with pinch grafts.

The principles involved are the construction of a "pilot" thumb on the back of the hand just proximal to the base of the first finger, by insertion of a small piece of bone



FIG. 4.—Pilot thumb transplanted to final position.



FIG. 5.—The skin on the palmar surface is supplied by radial nerve.



• FIG. 6.—The final digit after being reinforced by combined skin and bone graft from the chest wall.



under the skin in this situation, then to raise the bone and overlying skin as a small digit and skin-graft the raw area. Next, to transpose the "pilot" thumb and implant the bone into the existing base of the first metacarpal in such a line as will place the

skin covering the "pilot" on the palmar surface. A larger piece of bone is then implanted under the chest wall in a suitable position. The dorsum of the "pilot" thumb is then slit down the back and fixed to the chest wall with the new bone fixed to the base of the metacarpal and the bone of the "pilot" thumb. The hand is

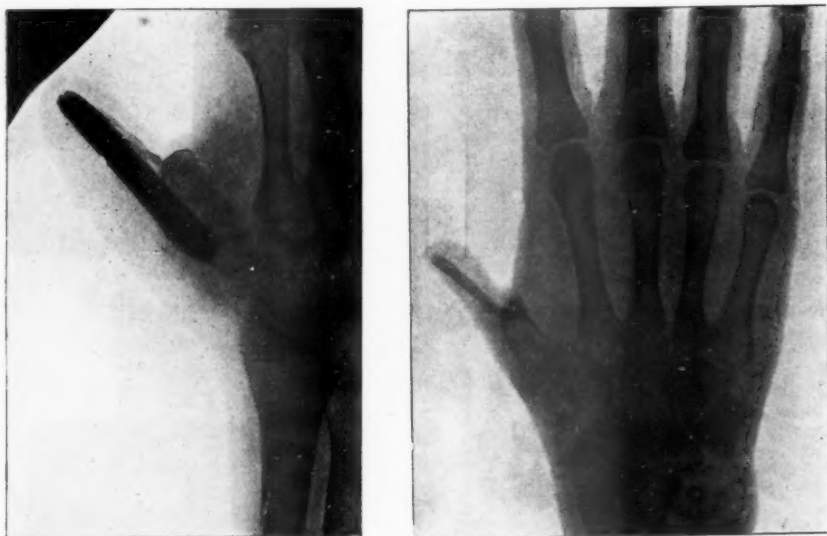


FIG. 7.—Radiograms showing the bone grafts used in the reconstruction.

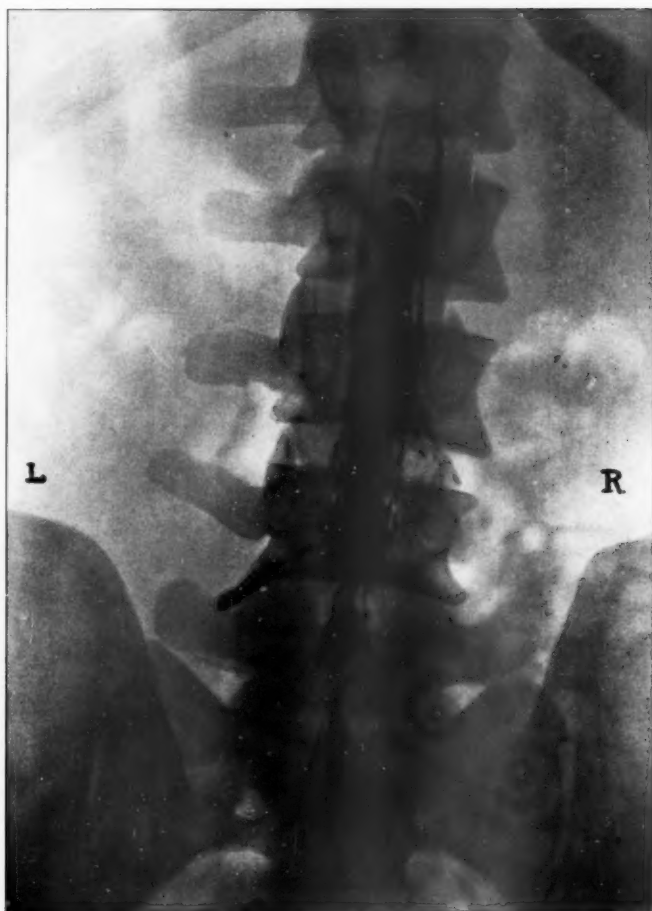
separated from the chest wall with sufficient skin to cover the dorsum of the new thumb.

Good function has developed and the boy can now use the new thumb for manual labour.

Intractable Sciatica due to Prolapsed Intervertebral Disc : Treated by Laminectomy.—NORMAN CAPENER, F.R.C.S.

This is an example of the type of case about which an increasing number of articles have appeared in the American medical press. In particular I must acknowledge my indebtedness to Love and Camp [1] of the Mayo Clinic.

In a paper I read at a meeting of the British Orthopaedic Association in 1934 I discussed the influence of certain spinal movements upon the cause of sciatica. As the result of radiological studies of normal spines, I stated that sciatica due to compression stresses upon nerve roots was more liable to occur in hyperextension but that traction stresses were most likely to be the cause of trouble when the lumbosacral spine was hyperflexed. I demonstrated the opening-up posteriorly of the intervertebral interval in hyperflexion and remarked upon the ease with which prolapse of the nucleus pulposus could occur in this position. Most cases of traumatic sciatica occur with a force exerted in the flexed position often associated



Postero-anterior view of spine after injection of 5 c.c. lipiodol. Note arrest of main mass at lower border of 4th lumbar vertebra, also filling of meningeal prolongation around 4th left lumbar nerve root.

CAPENER Intractable Sciatica due to Prolapsed Intervertebral Disc: Treated by Laminectomy.

with the lifting of heavy weights. One can quite understand the possibility of a portion of the disc being extruded like a pea out of a pod.

Although the treatment of this patient by laminectomy has been very successful I do not suggest that it is likely to be a common therapeutic measure. Having given other means a fair trial without relief then, in such intractable cases and after suitable investigation, it should be considered.

Concerning the technique of the operation, I have not attempted to remove the projecting portion of the intervertebral disc. To do so comfortably would involve extensive removal of the posterior vertebral articular facets. Holding strong views on the mechanical factors underlying spondylolisthesis [2] I have not been prepared to do this in the case of manual labourers. In the three cases that I have dealt with thus, of which the present case is one, the end-result has justified my procedure.

T. W., a railway engine-driver, aged 41, "sprained" his back at work in August 1935 and a short time later began to suffer severe pain in the right buttock and thigh. The pain was accentuated after exertion, but was relieved by lying down.

September 1935: When first seen, he had typical right-sided sciatica with homolateral scoliosis, rigid lumbar spine, gluteal wasting, and a diminished Achilles reflex. There were no sensory changes. No obvious cause could be found for the sciatica, and the X-ray findings were negative. During the next six months he received the usual conservative treatment, including radiant heat, massage, plaster jacket, sciatic nerve stretching, epidural injections, and manipulations under anæsthetic—all without lasting improvement.

In the summer of 1936 he had pneumonia, and the sciatica became much worse. The pain now involved the opposite side, and he was altogether in a very unhappy condition.

October 30, 1936: Lumbar puncture was performed at the level of the third and fourth lumbar vertebræ, with manometry, the pressure was normal, and there was the usual rise on jugular compression. A needle was now passed into the sacral hiatus, as for epidural injection, and novocain-saline solution was injected into the epidural space. There was a small rise in the intrathecal pressure, but not corresponding to the amount of fluid injected, thus suggesting a partial spinal block. The cerebrospinal fluid contained 60 mgm. per cent. of protein. Two days later 5 c.c. of lipiodol was injected into the theca at the first lumbar interspace, and radiographs were taken in the recumbent and erect positions. The evidence obtained by this means strongly suggested a constriction of the theca arising from the front of the canal in the region of the disc between the fourth and fifth lumbar vertebræ. Following the lipiodol examination the patient had very severe pain which had to be relieved by further lumbar puncture.

November 12: Laminectomy was performed on the fourth and fifth lumbar and first sacral vertebræ. The constriction at the level mentioned was amply confirmed; there was no pulsation below this level, and the posterior projection of the disc was verified. In addition, the constriction of the dura appeared to be circumferential in nature. This was widely opened up in the mid-line; the disc was not interfered with, and the wound was closed. Immediate and complete relief was experienced after recovery from the operation. All objective evidence of sciatica has disappeared. The man reports that since leaving hospital he has been back at his usual work, which occasionally involves coaling the furnace.

I have pleasure in acknowledging the painstaking radiological investigations carried out by my assistant Mr. Geoffrey Lillie, F.R.C.S. The illustration shown is one of many radiographs taken in different positions, supine and erect, in order to demonstrate a spinal filling-defect with lipiodol.

References.—1 LOVE and CAMP, *Proceedings Mayo Clinic*, August, 1936. 2 CAPENER, "Spondylolisthesis," *Brit. J. Surg.*, 1932, 19, 374.

Arthrogram to show Extent of Synovial Cavity After Synovectomy.

—JOHN P. HOSFORD, M.S.

Female, aged 19. In August 1931, synovectomy was performed on account of multiple synovial chondromata. At the operation the whole of the synovial membrane was removed from the front and middle of the knee-joint, also from the back on the inner side. A small portion was left on the outer side of the back of the joint.



January 1937 : The joint was distended with oxygen and an arthrogram taken. As the oxygen was run into the joint, at a pressure of 140 mgm. of mercury, the synovial cavity was seen to swell and fill up, as in the case of a normal joint. The arthrogram shows the synovial cavity to be of normal appearance, especially the subcureal pouch of the joint, which is of normal shape and size, having a smooth and even outline. Chondromata are seen at the back of the joint where the synovial membrane was not removed at the original operation.

Two Cases of Ocular Torticollis.—E. E. CASS, M.B., B.S.

I. Left ocular torticollis due to congenital muscle weakness (? of left superior rectus). Followed by divergent squint (convergence insufficiency in type.)

M. R. M., female.

History.—Glasses at age of 7, on account of myopia. First seen at St. Mary's Hospital at age of 8, right divergent squint noted.



FIG. 1a.—Normal position of head, with torticollis present.



FIG. 1b.—Normal position with head turned towards lower eye.



FIG. 2.—Looking away from the side of the torticollis. Vertical deviation least in this position.



FIG. 3.—Torticollis corrected. Right eye deviates up.

On examination.—Left torticollis present with very slight contraction of left sternomastoid. On straightening head, right eye deviates upwards. On looking to left, right eye goes upwards and inwards. On looking to right, the vertical deviation is practically nil.

Cover test: Right eye deviates upwards and outwards; left eye deviates outwards. *Vision:* Right eye, with glass, $\frac{6}{12}$ p.; left eye, with glass, $\frac{6}{18}$ p. Myopia of medium degree present. *Angle:* With torticollis present: Vertical deviation R/L = 3° ; with torticollis corrected, vertical deviation R/L = 8° . Lateral deviation



FIG. 4.—Torticollis corrected. Patient can now control vertical deviation.

3° divergent in every position. Binocular vision: Tendency to right macular suppression; feeble degree of fusion; no abnormal retinal correspondence. No convergence on near vision. Diplopia elicited with red and green goggles; greatest vertical deviation of images on looking up and to left.

Treatment.—Glasses and orthoptic exercises for one year. The patient was made conscious of squint by practising the attainment of diplopia with red and green goggles. She was also made to correct the position of her head. The binocular vision was improved and she was taught to correlate accommodation and convergence. [Exercises were also given to improve the co-ordinate movements of the eyes.

The accompanying photographs were taken after the lateral deviation had been cured, but with the vertical deviation still present.



FIG. 5.—Torticollis with contraction of sterno-mastoid and trapezius, also scoliosis associated with a vertical deviation of the eyes (case not shown at meeting).

Result.—No divergence. Convergence amplitude 50° . Can control upward movement of eyes except on extreme adduction of right eye. Binocular vision : Stereopsis.

II. Right torticollis and scoliosis associated with ocular muscle weakness (? of right superior rectus.)

History.—Squinted since birth. Normal labour. Has had remedial exercises for scoliosis.

Present condition (aged 14).—Right torticollis ; some contraction of right sterno-mastoid ; right shoulder higher than left ; scoliosis. Left eye markedly deviates above right eye ; deviation increases when head is straightened, and tilted to left. On looking to left, with torticollis uncorrected, eyes are most nearly level. On looking to right, with torticollis uncorrected, left eye deviates up markedly.

Angle : Vertical deviation L/R 18° and 3° divergent. On abduction of left eye 20° angle = L/R 6° and 2° divergent. On abduction of right eye 20° angle = L/R 30° and 2° convergent. Vision : Right and left vision $\frac{6}{6}$. (Normal vision emmetropic.) Cover test : Left eye deviates more markedly than right eye.

Binocular vision : True and abnormal retinal correspondence, with suppression. Right eye most markedly used for fixation. On fixing with right eye if an object is moved from above downwards on retina of left eye : There is an abnormal retinal correspondence at an angle of L/R 8° and 3° convergent. If an object is moved across the retina from below upwards, there is a true correspondence at L/R 18° and 3° divergent.

Treatment.—None to date, as patient cannot attend at present.

Comment.

There are two types of torticollis associated with deviation of the visual axes : (1) In which the torticollis is caused by the abnormal position of the eyes ; (2) in which the torticollis is probably the primary condition and the ocular deviation is secondary to it.

(1) In the purely ocular cases the torticollis is always slight and is not constantly present. There is usually only side flexion of the neck, and the chin is not rotated to the opposite shoulder as in cases of congenital torticollis. It is associated with a vertical squint (vertical deviation) of the eyes, accompanied by cyclophoria (rotation of the visual axes). The head is tilted towards the lower eye but at times it is turned towards the side of the lower eye instead of being tilted, and the eyes are deviated to the opposite side. When the eyes are deviated away from the side of the torticollis the vertical deviation is least, when they are deviated towards the side of the torticollis the vertical deviation is greatest ; also if the head is straightened or the torticollis over-corrected this vertical deviation becomes marked. All cases in the course of time become either divergent or convergent to some degree.

Diplopia may be complained of and in nearly all cases can be elicited by aid of the red and green diplopia goggles. Patients with a marked vertical deviation occurring in early life have no normal binocular vision. Normally both eyes are turned towards the object fixated, so that the image of this object falls on the maculae, and the two macular images are made one by the brain. In these cases it is impossible for the two eyes to be brought into a position where the visual axes are level, even by extreme head flexion. Abnormal retinal correspondence is found, especially when the vision in one eye is defective.

(2) Cases of ocular muscle defect associated with torticollis. In these cases—as in the accompanying illustration—the torticollis is marked, with rotation of the chin, and contraction of the sternomastoid. Facial asymmetry and scoliosis are also present. The ocular condition is often slight and may be missed entirely. The cause may be a central one ; it may lie in a labyrinthian anomaly producing changes in the tone of the ocular and neck muscles or the ocular deviations may be related to ocular motor reflexes excited by the contractions of the neck muscles. It is sometimes very difficult to ascertain which muscle is at fault ; often the condition is not confined to one muscle.

Treatment.—Cases of purely ocular torticollis lie in the hands of the ophthalmologist rather than of the orthopaedic surgeon. Exercises in binocular vision, co-ordinate movements of the eyes, and convergence, must be carried out and then, if necessary, followed by an operation.

The second type of case is rarely seen in an eye department and probably falls into the hands of the orthopaedic surgeon.

The following were also shown :—

(1) *Genu Recurvatum*. (2) *Congenital Fusion of the Subastragaloid Joint*.—C. LAMBRINUDI, F.R.C.S.

Cystic Disease of the Radius.—E. J. SMITH, M.B., B.S. (for ST. J. D. BUXTON, F.R.C.S.).

Unusual Defect of the Shoulder.—H. S. TAYLOR-YOUNG, F.R.C.S. (introduced by Mr. G. R. GIRDLESTONE).

Gross Patchy Rarefaction of the Ends of the Long Bones in a Case of Tuberculosis of the Hip.—L. W. PLEWES, F.R.C.S.Ed. (introduced by Mr. GIRDLESTONE).

? **Sciatic Scoliosis.**—V. H. ELLIS, F.R.C.S.

Arthritis of Elbow: for Diagnosis.—F. P. FITZGERALD, M.B.

Treatment of Fractures of the Neck of the Femur (cinematograph film.)—K. H. PRIDIE, F.R.C.S.

[May 4, 1937]

The following were shown :

(1) **Congenital Deformity of the Hip.** (2) **Lumbar Scoliosis: Case for Diagnosis.**—L. H. F. WALTON, M.R.C.S., L.R.C.P.

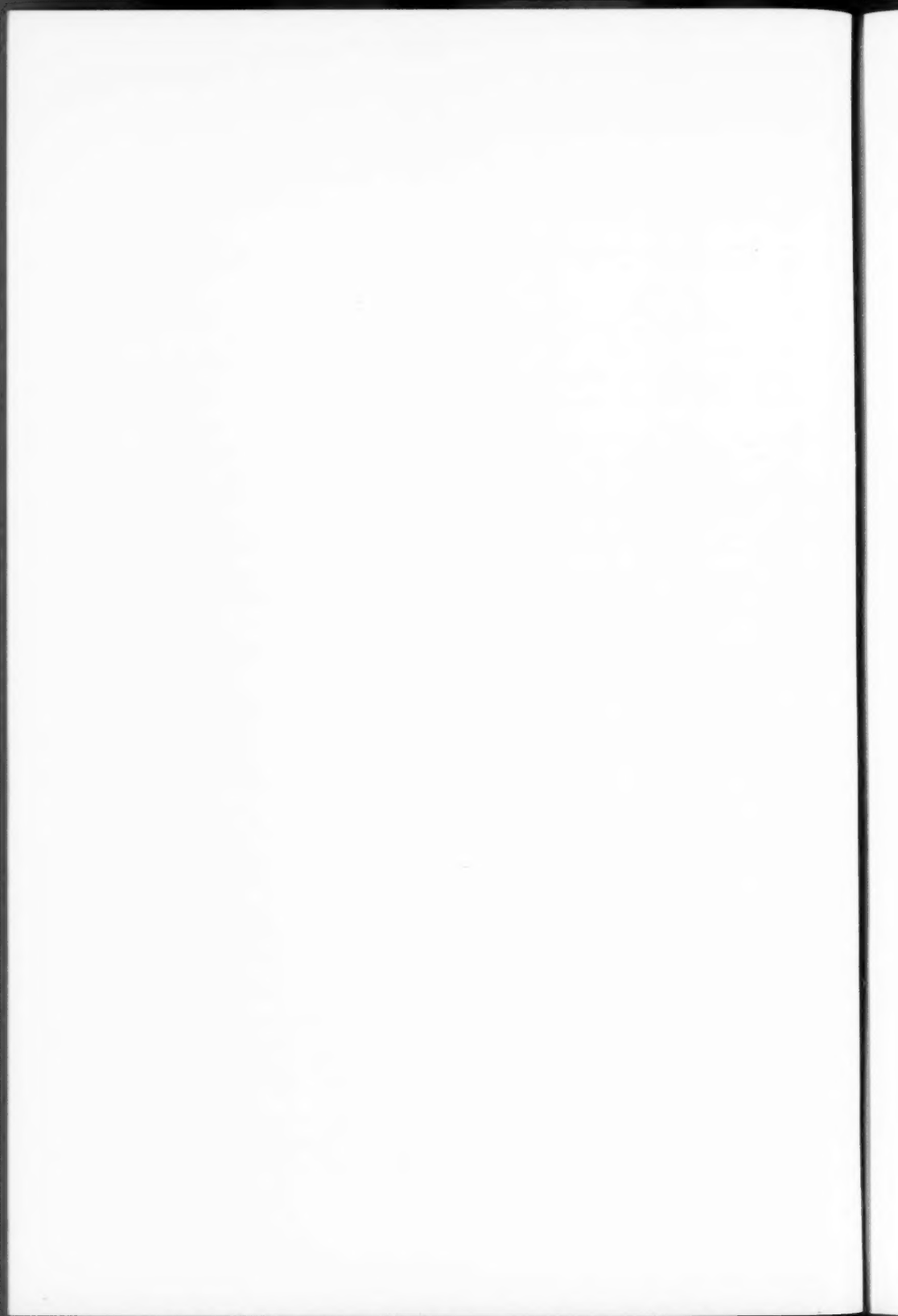
Destructive Lesions of the Knee-joint.—G. R. GIRDLESTONE, F.R.C.S.

Osteochondritis of the Patella and Tubercle of the Tibia occurring in the Same Patient.—J. H. CYRIAX, M.B.

(1) **Extra-articular Tuberculous Focus in the Region of the Knee.** (2) **Congenital Absence of the Fibula.**—J. A. CHOLMELEY, F.R.C.S.

An Operation of Historic Interest.—H. E. HARDING, F.R.C.S.

Spondylolisthesis in a Girl of 15 years.—H. J. SEDDON, F.R.C.S.



Section of Ophthalmology

President—W. H. McMULLEN, O.B.E., F.R.C.S.

[January 8, 1937]¹

Experimental Staining of the Retina in Life

[Preliminary Communication]

By ARNOLD SORSBY, F.R.C.S., A. ELKELES M.D. (Berlin),
G. W. GOODHART, M.D. and I. B. MORRIS M.B., B.Chir.

VITAL staining of the eye has been studied by Goldmann (1909), Schnaudigel (1913), Rados (1913), Seidel (1918), Fisher (1929), and Kuboki (1930) amongst others. Goldmann showed the presence of reticulo-endothelial cells in ocular tissues; systematic investigations, mainly with acid dyes, were carried out by other observers to determine what ocular structures stained with vital dyes. The comprehensive work of Fisher, in 1929, on the staining of the vessels in the iris and ciliary body, was applied by Kuboki in 1930, in the albino rabbit, for the study of the choroidal vessels. He found that they reacted in very much the same way as Fisher had shown for the vessels of the iris and ciliary body; he further considered it possible that the basic dyes gave a rapidly transient staining of the retina itself.

In the course of our work it was found that the basic dyes that had been used to obtain vital staining of the brain, were all highly toxic when injected intravenously and we found it difficult to determine whether any transient staining visible ophthalmoscopically could be obtained in an animal that was not experiencing terminal throes. Such staining as was obtained was frequently intensified after death, and here again the question of supra-vital staining assumed importance. Most of the dyes, however, became rapidly decolorized in the fundus, almost whilst they were being injected into the blood-stream. One point of interest was that an injection of the leuco-base of methylene blue, prepared by the rongalite method, was followed by a deep blue colour in the fundus, steadily becoming decolorized. The difficulty was to obtain observations of any duration, owing to the toxicity of these agents. Light green S. F. was found to be well tolerated, but the colour disappeared rapidly. As the experiments suggested that the decolorization presented a process of reduction to the leuco-base, the question arose whether the damaged retina would be able to reduce the dyes as effectively as the normal retina. Experimental degeneration of the retina was produced by the intravenous injection of septonod, when pigmentary changes could be observed after four days, becoming well established within a fortnight. Rabbits thus treated showed the same transient staining of the fundus as the normal rabbit when treated with 12 c.c. of 10% light green solution injected intravenously, but in contrast to the normal rabbit, such rabbits also showed staining which appeared half an hour subsequently and persisted for about twenty-four hours. It was further found that the same result could be obtained by the intramuscular injection of 10 c.c. of the 20% solution, the colour appearing one and a half hours later; no staining of the fundus could be obtained in the normal rabbit by intramuscular injection.

On the suggestion of Mr. L. H. Savin these experiments were repeated on a rabbit in which the retinal damage was produced by cauterization of the sclera instead of

¹ The publication of this report has been delayed in order to include the coloured illustrations

the chemical damage produced by septojod. In such a rabbit an intravenous injection of the dye stained the damaged area and some adjacent retina, but left the rest of the fundus unstained, as also the fundus of the normal fellow eye: Fast acid violet, 15 c.c. of the 1% solution, injected intramuscularly in septojod rabbits also gave coloration of the fundus, the colour being deep purple. The brains of rabbits treated with light green and fast acid violet stained a green and deep purple colour respectively. The histological examination of the eyes of a rabbit treated with septojod and light green showed the dye present in the retina. As with vital staining in other tissues, difficulty was experienced in fixing the dye and for the present we have confined ourselves in demonstrating the dye in the freshly teased retina.

The seven rabbits demonstrated before the meeting were chosen to illustrate the following points:—

- (1) Septojod degeneration of the retina.
- (2) Late light green staining of the retina in a rabbit with septojod degeneration of four days standing.
- (3) Much more intense light green staining of a rabbit's retina with septojod degeneration of three weeks standing.
- (4) Non-staining of the retina in the normal rabbit with the injection of light green in the same way as rabbits 2 and 3 were treated. (Intramuscular injection of 15 c.c. of the 20% solution, five hours before the demonstration.)
- (5) Staining of the retina damaged by cautery and non-staining of the rest of that retina and of that of the fellow eye, in a rabbit treated with intramuscular injection of light green.
- (6) and (7) Purple staining of the fundus with an intramuscular injection of 15 c.c. of 1% fast acid violet in rabbits showing septojod degeneration.

We wish to acknowledge our indebtedness to Mr. R. T. M. Haines, M.A., of Messrs Crookes Laboratories Ltd., for his valuable help with the chemical aspects of the work and to his firm for supplying the dyes. To Dr. Bessie Cadness we are also obliged for her helpful advice on chemical problems. To the London County Council we are grateful for the facilities offered to us at St. Mary Abbots Hospital for the carrying out of the work recorded. We are particularly obliged to Dr. J. A. H. Brincker for the kindly interest he has taken in this work.

Discussion.—Mr. EUGENE WOLFF said that there had appeared in the *American Archives of Ophthalmology* reports of cases in which after the long continued use of a certain drug there was an accompanying staining of the fundus. It was decided that the dye was in the vitreous. He asked whether any of the cases described in this paper were looked at with the eye opened and the vitreous removed.

Mr. SORSBY (in reply) said he thought that Mr. Wolff's reference was to clinical cases published in the *American Archives of Ophthalmology* (1936, N.S. 16, 443), accompanied by a coloured plate showing blue fundi. That plate had reference to the cases of four patients who were treated for uro-genital tuberculosis by means of methylene blue; they were given methylene blue by the mouth for four years, and the fundi assumed a blue colour. The authors (A. Gerber and R. K. Lambert), considered that the blue coloration was due to staining of the vitreous. He (Mr. Sorsby) and his collaborators had opened a number of eyes, and in each case the vitreous and the lens was unstained, while the aqueous was sometimes stained, sometimes not. Intravenous injection of the dyes which they had used was more likely to cause a staining of the aqueous than when given in any other way. There was evidence that with basic dyes the staining in the brain was in its nerve elements, and in the same elements in the eye, namely the retina. There was histological evidence that in the case of acid dyes the dye was mobilized in the choroidal plexus, and one expected it to be in the ciliary body and choroid—and not in the vitreous—in the case of the eye.

The problem was to find a group of dyes which would reach the nervous tissue. Those dyes should not be toxic, nor should they cause any local damage.

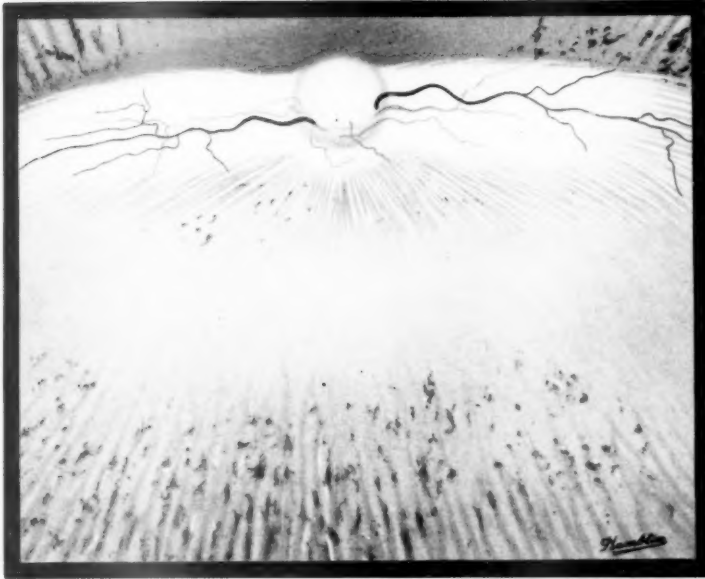
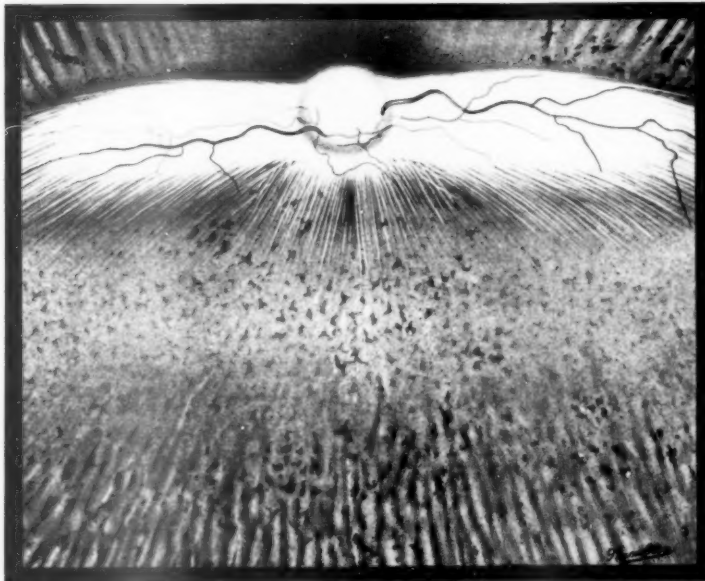


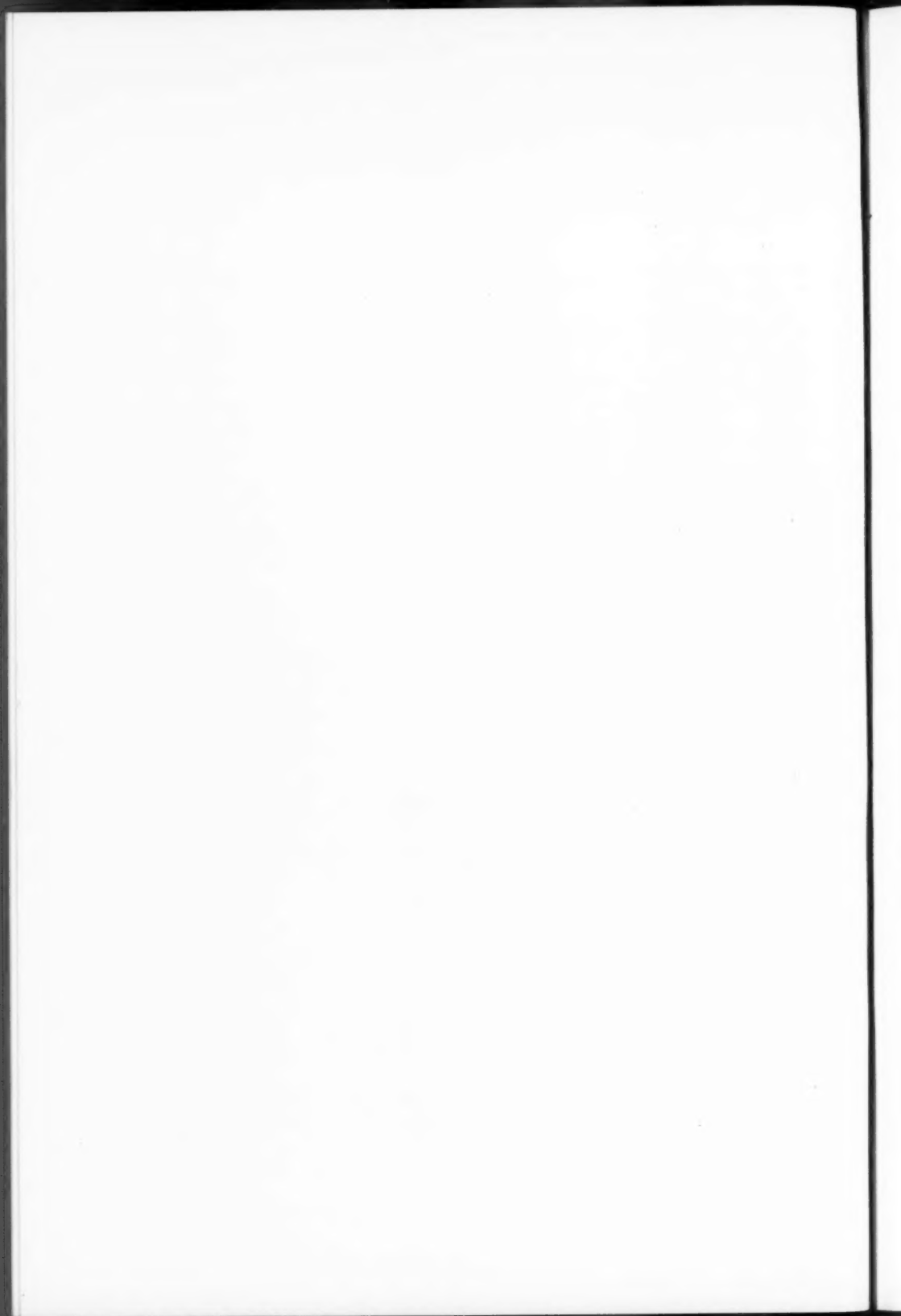
FIG. 1.—Rabbit's fundus showing pigmentary degeneration of the retina caused by intravenous injection of septonod.



John Bale Sons & Carnow Ltd London.

FIG. 2.—The same fundus as in Fig. 1 after intravenous injection of light green S.F.

SORSBY, ELKELES, GOODHART, AND MORRIS. *Experimental Staining of the Retina in Life.*



[June 11, 1937]

The Epithelial Growths of the Conjunctiva and Cornea

By E. F. KING, F.R.C.S.

THERE would appear to be no essential difference in the pathology of the epithelial growths found on the conjunctiva and the cornea and, in fact, far the most usual site for the carcinomata is the limbus—the border-line between the two.

The purpose of this paper is to review briefly these growths, to illustrate them by drawings of recent sections from the Pathological Department of the Central London Ophthalmic Hospital, and to consider their treatment.

These tumours may be considered as benign or malignant, and in most cases it is possible to give a definite pathological diagnosis; however, this distinction is not sharply defined, and it is certain that the more innocent do, at times, assume malignant properties.

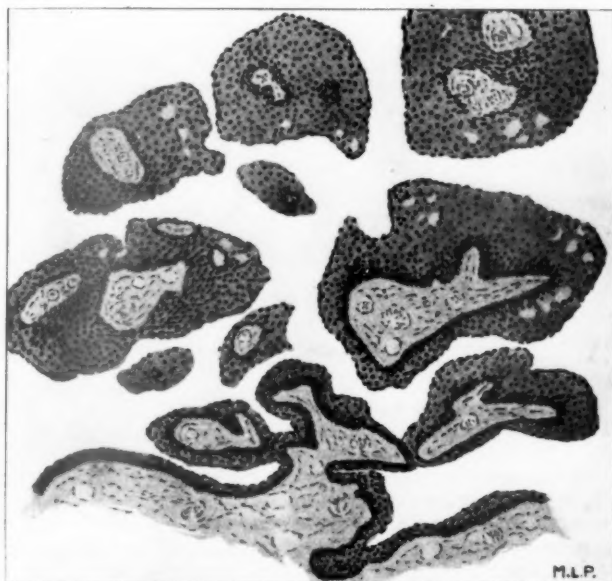


FIG. 1.—Simple papilloma of the conjunctiva.

To consider firstly the innocent tumours :—

(a) *Papillomata*.—These are most frequently seen in the fornices and on the caruncle, and have the appearance of small raspberries. Pathologically, the papilla consists of a delicate stroma, in which are thin-walled vessels, covered by stratified epithelium, the cells of which are regular in size and staining reactions. Beneath the papilla, and continuous with its central core, is seen a layer of new fibrovascular tissue. These tumours have a marked tendency to recur locally after removal, as do similar tumours in the urinary tract, and on rare occasions may become malignant (fig. 1).

(b) *Epithelial plaques*.—The other innocent tumour is the epithelial plaque. This is of interest and not common. It is seen on the conjunctiva or cornea, as a well-defined area of epithelial hyperplasia, the cells of which are of the "prickle" type, superficially keratinized. Parsons regards this growth as congenital and in the nature of a dermoid. Lister and Hancock, in 1903, reported four cases, three wholly on the conjunctiva and one partly on the cornea. They considered these analogous to callosities on skin epithelial surfaces, i.e. hyperplasia of the horny layers. The section I am showing covers the whole cornea and overlaps the conjunctiva. There are many layers of epithelial cells regularly arranged. Embedded between the epithelial cells are a number of areas of delicate fibrous tissue and vessels, and beneath them—superficial to Bowman's membrane, which is largely intact—a well-marked sheet of young fibrovascular tissue. There is no infiltration of the corneal stroma. Consideration of this section, and of the illustrations of other reported cases, incline one to the view that the epithelial plaque may be a variety of sessile papilloma in which the stroma is minimal; for the subepithelial mesoblastic hyperplasia, which is a feature of all papillomata, is evident, and the central cores of fibrovascular tissue are present, though not marked (fig. 2).



FIG. 2.—Epithelial plaque of conjunctiva and cornea.

To consider now the malignant epithelial growths:—

Rodent ulcer apparently never involves the eye primarily, so will not be included.

Epithelioma.—De Schweinitz has stated that epithelioma is more commonly secondary to lid involvement than primary in the eye itself, an observation which would, I think, receive very little support to-day.

The limbus is the most usual site for these growths, for here there is a transition in epithelial structure, limited papillae are usual, and actual downgrowths of surface cells into the subepithelial tissues are normally seen; but there have been a number of cases reported in which the growth is wholly on the cornea, as in fig. 4. Epithelioma on the conjunctiva, at a distance from the limbus, appears to be the result of malignant changes in a papilloma.

The tumour is most frequently seen in the interpalpebral space, particularly on the temporal side—i.e. in the area most exposed to trauma—and several cases have been reported following penetrating wounds, but this can hardly be a factor of importance, for the limbus is the most usual site for operation section which is, happily, not followed by the growth.

Occurrence under 40 years of age is unusual, and men are more commonly affected than women. Few aetiological factors have been elicited. Tudor Thomas (1930) has reported a case in a worker in fuel dust which contained 6% of pitch, a substance known to predispose to cutaneous papillomata, and Treacher Collins (1928) a generalized warty condition of the conjunctiva, apparently not definitely malignant, after

frequent and prolonged exposure to X-rays. Contagion appears to play no part in man, though it is interesting to note that Bevan, in 1925, reported six cases of carcinoma of the conjunctiva in one herd of Hereford cattle in Rhodesia.

The growth, which is sometimes pigmented by the normal pigment cells at the limbus, at first resembles a limbal dermoid, but later ulcerates and bleeds readily on manipulation. Bowman's membrane offers considerable resistance and for a time the mass remains superficial to it; later this yields and infiltration occurs along the lymph spaces around the corneal lamellæ, providing, as Treacher Collins has pointed out, a notable example of Sampson Handley's centrifugal lymphatic permeation of carcinoma cells. The sclera forms a dense barrier and becomes eroded rather than infiltrated. On reaching Tenon's capsule the growth extends rapidly, and in some cases completely surrounds the globe. Intra-ocular extension is seen in a high proportion of advanced cases, occurring along the anterior perforating vessels and Schlemm's canal or, when Tenon's capsule is involved, by way of the vortex vessels.

Involvement of the pre-auricular and submaxillary glands is late, and any enlargement detected may be septic, rather than malignant, when there is ulceration of the primary growth. There appear to have been only a few authentic reports of generalized metastasis and in some of these no microscopic diagnosis was made, which suggests that they may well have been cases of sarcoma.

Microscopically the growth consists of stratified epithelium and stroma, in papillomatous formation. A marked inflammatory cell infiltration is usual. The following points are characteristic of malignancy :—

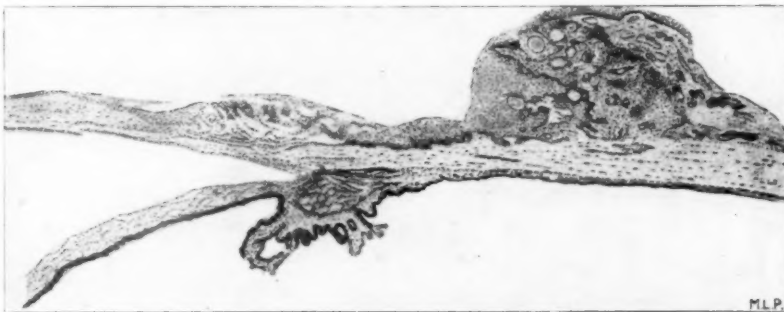


FIG. 3.—Squamous carcinoma at limbus.

(a) Variation in size and chromatin content of the epithelial cells, in some of which the nucleus is fragmented and degenerate while in others active mitosis is seen.

(b) Penetration of epithelial cells into the underlying tissues, though the dense structure of the outer coat of the eye prevents this until a late stage; a more usual appearance is actual erosion and loss of substance of the cornea and sclera, without infiltration. Further, it must be remembered that some dipping of the epithelium is not unusual at the normal limbus.

(c) The presence of characteristic cell nests, which are seen in the fibrous stroma of the growth rather than in the underlying structures.

(d) An inflammatory cell infiltration in and around the mass, even where there is no secondary infection consequent on ulceration (figs. 3, 4, 5).

Carcinomata.—In conclusion I would like to consider the treatment of the carcinomata.

When the cornea is extensively involved or the growth has penetrated the globe

or, in fact, in any case in which the function of the eye is irrevocably lost, excision or evisceration is clearly indicated.

If the growth is in the early stage of a small limbal tumour most surgeons are agreed that more conservative treatment is permissible, though some apparently advise excision of the eye in all cases in which the diagnosis is made, provided the other eye is sound; that this is so is shown by the number of eyes submitted for

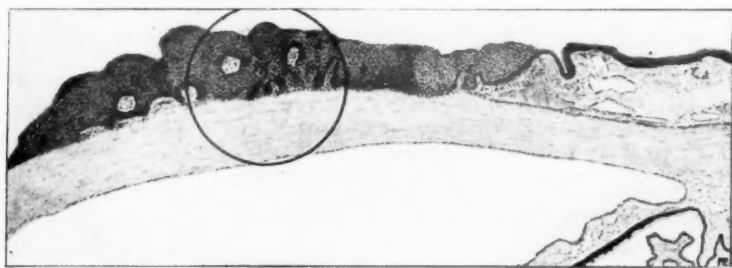


FIG. 4.—Carcinomatous changes in a papilloma of the cornea.

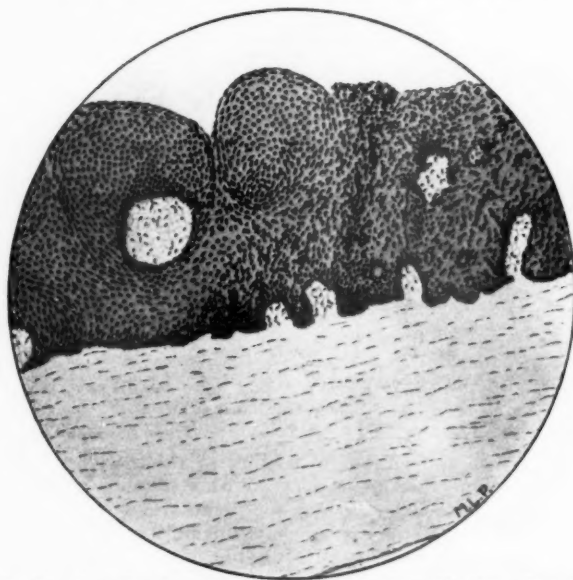


FIG. 5.—Area of section shown in fig. 4, under higher magnification. The cells on the left are innocent, but on the right side malignant changes have occurred.

pathological examination in which the growth is relatively small. Furthermore, in the last edition of Fuch's "Diseases of the Eye" (1933) the statement is made that "an eye with carcinoma at the limbus is unconditionally destined for enucleation, even when it still sees, since a clear extirpation is not possible with such tumours".

With regard to the more conservative lines of treatment local excision, cauterization, and X-rays, either alone or in combination, have been tried, with variable success.

Radium appears to offer an efficient and simple treatment, which is completely successful in the majority of cases and would seem to be particularly indicated in this condition, in which an early diagnosis—probably earlier than that of carcinoma in any other site in the body—is the rule, and glandular involvement and metastases are late.

Treacher Collins, Harrison Butler (1932), Roy Ward (1932), and Stallard (1933) in this country, and a number of surgeons abroad, have all published results of the treatment of epibulbar growths by radium, most of which have been highly satisfactory.

In general the technique has been the application of unscreened radium—whereby, of course, β radiation is largely used—to the surface of the growth for relatively short periods, the treatment being repeated at intervals if necessary. If the mass of the growth is considerable it appears desirable first to remove the greater part of it, but if it is small, the principle of no surgical interference before radiation is better adhered to; for the latter reason, also, biopsy is undesirable in most cases. This method is technically simple and with it the risk of radiation cataract is said to be minimized.

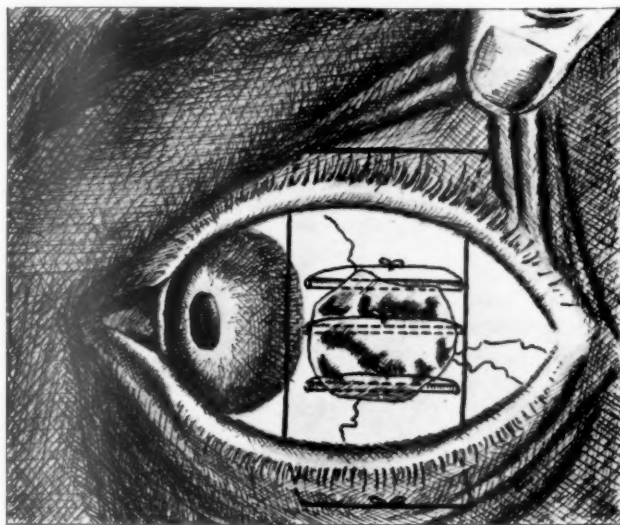


FIG. 6.—Method of insertion of radon seeds in the two cases of limbal carcinoma described.

During the last eighteen months I have had the opportunity of treating two cases of limbal carcinoma by means of radium. The technique employed (fig. 6) was suggested by Mr. Stanford Cade at the Westminster Hospital, and consisted in the insertion, for forty-eight hours, of three radon seeds, each of 1.5 millicuries, screened with 0.3 mm. of platinum. The seed was ordered slightly longer than the growth in its widest part, and to each end of it was attached a silk thread. A passage for the seed was made in the episcleral tissues beneath the growth by a Nettleship punctum dilator. The three seeds were inserted parallel, and when in position were secured by tying the thread at each end over the growth. Finally a mattress suture was inserted in the lids over the growth to hold them in apposition; by this means displacement of the seeds by the lids was avoided, and both patients remained quit

comfortable during the time they were in place. So far the results in both cases have been good. In the first (fig. 7) no abnormality is now discernible, and it is impossible to detect the site of the growth; in the other, which was shown by Mr. A. F. MacCallan at a meeting of this Section in October 1936, the tumour, has disappeared, though some scarring and pigmentation remain locally (fig. 8).

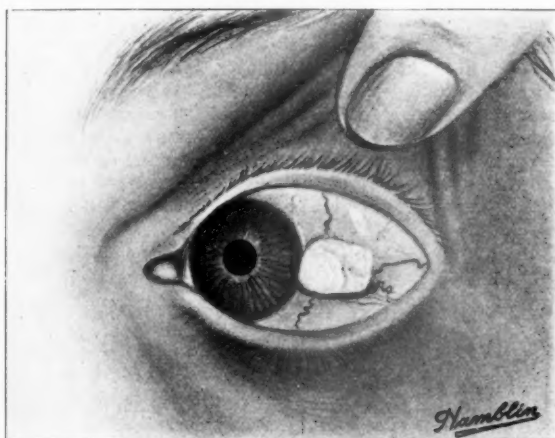


FIG. 7.—Case I. Limbal carcinoma. (Before treatment.) Case successfully treated by radium.

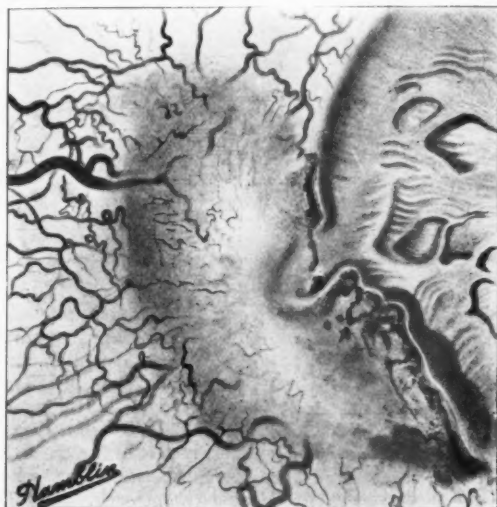


FIG. 8.—Case II. Limbal carcinoma successfully treated by radium

Radiation cataract has been reported by many observers after the use of radium in or near the eye, though there appears great individual variation in the dosage required to produce this and in the time of onset following exposure. It is probably true that in the method I have described, in which the more penetrating gamma rays are employed, there is greater risk of this than with the superficially applied beta rays. Mr. Cade, however, was of the opinion that with the dose used in these cases the risk to the lens was very slight, and there is certainly no suggestion of any opacity at present, though, of course, no final opinion can be considered on two cases at such an early date. I mention this method to show that interstitial radiation of epibulbar growths, which by some has been thought to present considerable technical difficulties, is quite feasible and appears to be therapeutically effective.

BIBLIOGRAPHY

- BARROW, S. C. (1925), *Radiology*, **4**, 54-55.
 BENEDICT, W. L. (1929), *S. Clin. North America*, **9**, 813-822.
 BEVAN, E. W. (1925), *Tr. Roy. Soc. Trop. Med. and Hyg.*, **19**, 153-155.
 BUTLER, J. H. (1932), *Brit. J. Ophthalm.*, **16**, 152-155.
 CASTROVIEJO, R., and CASTROVIEJO, R. Jr. (1931), *Am. J. Ophthalm.*, **14**, 757-768.
 CLARK, W. L. (1916), *J.A.M.A.*, **67**, 17.
 COLLINS, E. T. (1928), *Tr. Ophthalm. Soc. U. Kingdom*, **48**, 83-85.
 COOVER, D. H. (1920), *Am. J. Ophthalm.*, **3**, 683.
 COSGROVE, K. W. (1933), *South. M. J.*, **26**, 326-330.
 CRISP, W. H. (1917), *Colorado Med.*, **14**, 273.
 De SCHWEINITZ (1913), *Arch. Ophthalm.*, **42**, 373-379.
 Id. (1913), *Tr. Am. Ophthalm. Soc.*, **13**, 508-515.
 FRANCIS, L. M. (1921), *Arch. Ophthalm.*, **50**, 331.
 FREIMAN, G. (1932), *Am. J. Ophthalm.*, **15**, 1157-1164.
 FEJER, J. (1929), *Am. J. Ophthalm.*, **12**, 484-486.
 GANAGHAN, E. F. (1921), *Am. J. Ophthalm.*, **4**, 717.
 GOULDEN, C., and STALLARD, H. B. (1932), *Tr. Ophthalm. Soc. U. Kingdom*, **52**, 47-56.
 HEYMANS, J. (1929), *Arch. d'ophth.*, **46**, 48-55.
 JANEWAY, H. H. (1920), *Arch. Ophthalm.*, **49**, 156.
 JUDD, J. H. (1929), *Arch. Ophthalm.*, **2**, 133-137.
 KEITH, D. Y., and KEITH, J. P. (1922), *Am. J. Roentgenol.*, **9**, 337-340.
 KOELLNER (1917), *Arch. Ophthalm.*, **46**, 130.
 NEW, G. B., and BENEDICT, W. L. (1920), *Am. J. Ophthalm.*, **3**, 244.
 PAPOLCZY, F. Von (1932), *Arch. f. Augenh.*, **105**, 537-541.
 QUIGLEY, D. T. (1931), *Nebraska M. J.*, **16**, 192.
 SORIA, M. (1932), *Bull. et mém. Soc. franç. d'ophth.*, **45**, 112-115.
 STALLARD, H. B. (1933), *Brit. J. Ophthalm.* (Monograph Supplement VI).
 STIEREN, E. (1918), *Am. J. Ophthalm.*, **1**, 278.
 TERRIEN, F. and COUSIN, G. (1931), *Bull. et mém. Soc. franç. d'ophth.*, **44**, 279-283.
 Id. (1931), *Arch. d'ophth.*, **49**, 622-631.
 THOMAS, J. W. T. (1930), *Proc. Roy. Soc. Med. (Sect. Ophthalm.)*, **23**, 20-21.
 VEASEY, C. A. (1920), *Am. J. Ophthalm.*, **3**, 113.
 P. VEIL, (1928), *Arch. d'ophth.*, **45**, 506-514.
 VILLARD, H., and DEJEAN, C. (1933), *Arch. Soc. d'ac. méd. et biol. de Montpellier*, **14**, 464-466.
 VILLARD, H., DEJEAN, C., and TEMPLE, J. (1932), *Arch. Soc. d'ac. méd. et biol. de Montpellier*, **13**, 455-458.
 WARD, R. (1932), *Proc. Roy. Soc. Med.*, **26**, 1515-1532.
 WEYMANN, M. F. (1932), *Am. J. Ophthalm.*, **15**, 310-312.

Discussion.—Mr. T. HARRISON BUTLER said that the first case of the kind which he remembered seeing was one of pedicled tumour of the limbus. Microscopic examination of part of the growth showed it to be a hæmangioma; it was illustrated in his (the speaker's) book on the slit-lamp. Sprays of growth were seen passing into the cornea, and this, he thought, indicated that the growth was malignant. The patient was sent to the Radium Institute, and after two applications of radium the growth disappeared.

Another case was that of Clara Smith, of which there was a coloured drawing in his (the speaker's) book. The late Mr. Treacher Collins and others saw the case and considered that the growth was an epithelioma. It was pigmented, not raised above the surface, but implicating the cornea over several millimetres. He first saw the patient about twelve years ago. She too was sent to the Radium Institute and received several applications. He had seen her from time to time since, the last occasion being a month ago, and she was perfectly cured. But when the eye was examined with the slit-lamp it could be seen that some of the pigment had remained behind. One must therefore conclude that the radium did not necessarily destroy the pigment.

Speaking from memory, he had had about ten cases of the kind treated at the Radium Institute by surface irradiation. In three there was no recurrence ten years afterwards.

Mr. Jameson Evans had asked him to see a man who had had X-ray treatment extending over a long time for the purpose of curing an extensive naevoid condition of his face and had developed typical radiation cataract. Vogt, in his Atlas, gave a description of radiation cataracts, and, as far as the speaker could see, there was no difference between the result (in this respect) of X-rays and that of radium. But, used in the way required to cure these eye tumours, the risk of causing radiation cataract was infinitesimal. He could not understand how, at the present day, anyone could suggest that eyes of the kind under discussion should be enucleated.

Mr. A. D. GRIFFITH, with regard to the risk of producing radiation cataract, which was the bogey of the treatment of these cases by irradiation, asked whether Mr. King had tried using very much heavier doses of radon for a shorter time—for instance 80 millicuries for an hour. Such a method was, he thought, less likely to cause cataract than a smaller dose longer continued. Cataract, if it occurred, came on three or four years after the exposure; the interval since the treatment in the cases described to-day was too short to know whether cataract would appear.

In a case of rodent ulcer of the upper lid which he had treated with radon six years ago the first sign of lens change was a change in the refraction. The patient has been hypermetropic, +2, and nothing happened for 2½ years. He then became myopic, reaching -2.5. Six months later the lens became opaque. The dose had been 6 mc. for five days. He suggested that the refraction should be watched in cases treated by irradiation.

Mr. KING (in reply) said he thought that, technically, the method employed in the two cases described was as simple as that used at the Radium Institute. Unscreened radium was applied for a considerable time, up to an hour, and it might be necessary to repeat it on several occasions.

Section of Obstetrics and Gynæcology

President—CLIFFORD WHITE, F.R.C.S.

[February 19, 1937]

A New Type of Nitrous-oxide Machine for Self-induction of Analgesia during Labour

By J. CHASSAR MOIR, M.D.

I WISH to bring to your notice a nitrous-oxide machine intended for self-induction of analgesia during labour. This new apparatus differs from machines of the automatic type previously in use by supplying pure, instead of diluted, nitrous-oxide gas.

Labour pains are intermittent and there is but short warning of their approach. The success of nitrous-oxide analgesia in labour is therefore largely dependent on the amount of gas which a woman can inhale in the short warning period of about twelve seconds which precedes the climax of each pain.

If pure nitrous oxide is inhaled for even ten or twelve seconds (two deep breaths) an appreciable analgesic effect is produced in most patients, and this effect is more intense and considerably more rapid in its onset than is the case with the usual 35% gas-air mixture inhaled for as long as thirty seconds. Pure gas is thus more suited to the needs of a patient in labour than is a gas-air mixture.

In order to ensure safety, the new machine embodies a device which makes it impossible for a patient to obtain more than two deep breaths of gas at one time. The machine consists essentially of a bag which acts as a reservoir. The bag can be quickly emptied, but it refills at a very slow rate—a full minute elapsing before it becomes replenished. When full, the bag automatically cuts off its own supply, thus preventing waste of gas. The apparatus, made by A. Charles King, Limited—to whom I am deeply indebted for help—is simple, efficient, comparatively cheap, and economical in use.

The machine can be used whenever labour pains begin to distress the patient, and instruction for its use should be given early in labour. With the first warning of a renewed pain the patient should press the mask to the face and empty the bag in two (or not more than three) deep, moderately quick breaths. The mask should then be laid aside in readiness for the next pain. The machine can be used throughout the greater part of labour. In most cases, however, the final stage of delivery is best conducted with the aid of a more powerful anæsthetic, such as chloroform, administered by the Young-Simpson inhaler.

As in the case of machines delivering a gas-air mixture, the new apparatus may on rare occasions cause cyanosis. A special watch has been kept for this, and in 120 cases some degree of intermittent cyanosis has been seen five times; in none of these cases did any harm result to mother or child. In this connexion it must be remembered that some women during strong bearing-down efforts show slight cyanosis quite apart from administration of gas. The possibility of producing a slight and repeated anoxæmia makes it important, however, to avoid gas, or gas-air administration to patients suffering from respiratory embarrassment.

The new machine has been in use in the obstetrical wards of Hammersmith Hospital (British Post-graduate Medical School) and has been found to give results which are a decided improvement on those previously obtained by the use of a machine delivering a gas-air mixture. I can commend this apparatus as providing a simple and efficient means of relieving the severity of the pains of labour.

Modified Mayo Operation for Procidentia

By EVERARD WILLIAMS, M.D.

IN the experience of Gray Ward the weak point in the Mayo operation for prolapse is that an otherwise perfect result may be impaired by the subsequent development of enterocele or high rectocele, due to the extensive stretching of the posterior segment of the fascial supports, so frequently found in procidentia.

In the modification here described considerable attention is paid to the dissection of the posterior segment and the definition of the layers of fascia. This is accomplished by the inclusion of the necessary colpoperineorrhaphy in one step with the hysterectomy and interposition, and the complete reversal of the order of procedure in the classical operation.

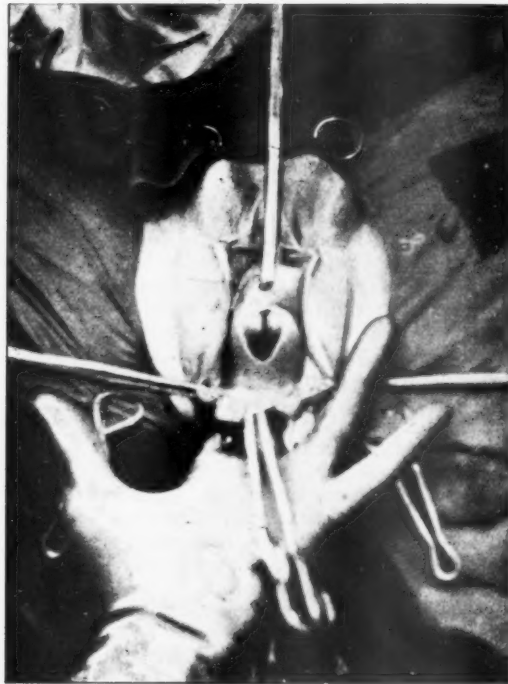


FIG. 1.

The dissection is begun from behind, at the posterior commissure of the vagina, and not from the front, below the urethra, as in the technique employed by Gray Ward. However, the Gray-Ward technique of excision of the pouch of Douglas, and approximation of the utero-sacral ligaments is followed, with an addition designed to direct the force of impact of the intra-abdominal pressure obliquely on to the levator ani muscles. This is accomplished by the suture of the already

approximated utero-sacral ligaments to the fascia covering the levator ani muscles on their deep aspect.

TECHNIQUE OF THE OPERATION

The operation is conducted under basal anaesthesia with avertin solution supplemented by ether-chloroform mixture. The cervix is retracted upwards, as far as is possible, by an assistant.

An incision is planned as in routine perineorrhaphy. The dissection is carried laterally until all cellulitic adhesions have been freed, and loose cellular tissue is reached; it is carried upwards until the pouch of Douglas is freed from its attachment to the vagina.

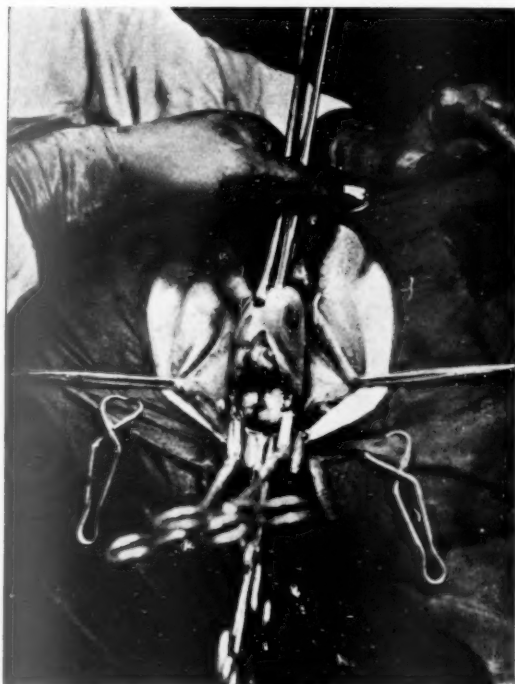


FIG. 2.

In its conclusion, this dissection is carried out by the fingers of the operator's hand. At the conclusion of this stage the posterior and postero-lateral vaginal walls are free of their attachments.

The pouch of Douglas is opened and the utero-sacral ligaments are seized in strong angled clamps and divided adjacent to the uterus. The uterus now descends appreciably, and is rendered more mobile, a point which aids the subsequent dissection. A small pack, with tape attached, is inserted into the opened pouch of Douglas, and this stage of the operation is concluded.

The steps of the classical Mayo operation are now followed until the broad ligaments have been ligated with mattress sutures.

The pouch of Douglas is now excised, redundant tissue removed, and a purse-string suture of catgut used to transfix the peritoneal edges. After suturing Mackenrodt's ligaments together in the mid-line, the posterior extensions of this fascia which joins with the utero-sacral ligaments, are similarly approximated by separate suture.

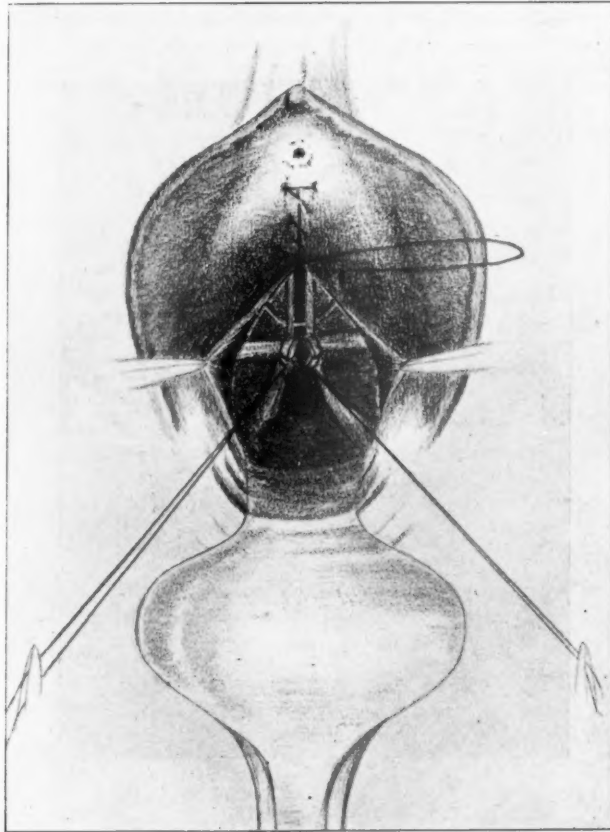


FIG. 3.—Mackenrodt and utero-sacral ligaments tied together in mid-line and joined to posterior ends of the broad ligaments. Pouch of Douglas seen posteriorly between the utero-sacral ligaments.

Attention is now paid to the perineal part of the wound. Three deep sutures are passed through the levatores ani muscles, about $\frac{1}{2}$ in. to $\frac{3}{4}$ in. apart (using the Reverdin needle) and taking care to obtain a good bite of the muscle. The utero-sacral ligaments are now securely approximated, from before backwards, by continuous suture,

and in such a way that their inferior surface is incorporated in the already approximated levatores ani muscles, on their superior surface. If high rectocele is present, the torn ends of the fascia propria are sought and incorporated in the suture line, with the utero-sacral fascia.

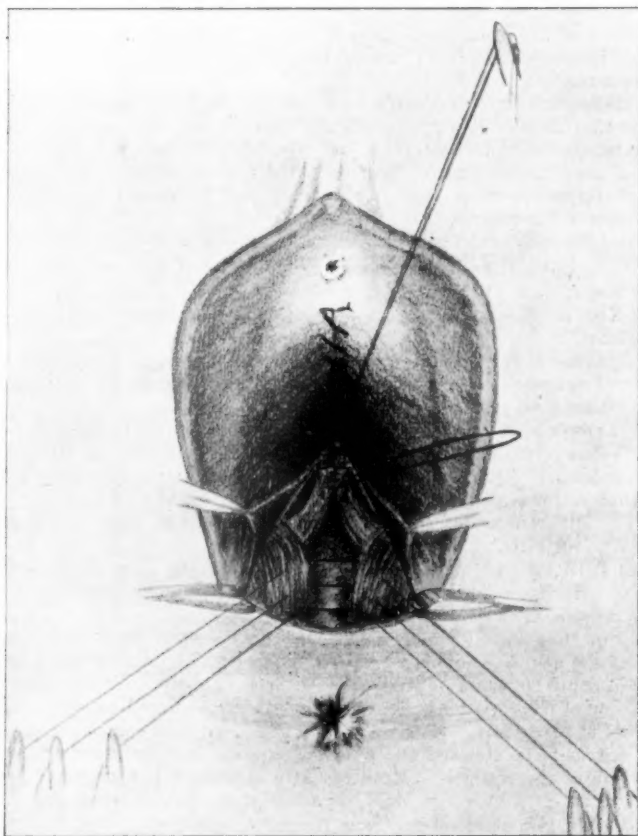


FIG. 4.—Pouch of Douglas closed and utero-sacral ligaments sutured together beneath it. Sutures in levatores ani muscles held in forceps while the approximated ligaments are transfixed through them.

At the conclusion of the operation, the urethral orifice is seen to be in its normal situation, and the depth of posterior vaginal wall is from 2 to 3 in. in length. The wound is closed without drainage, a self-retaining catheter is inserted, and as soon as the patient is in bed, the residual avertin solution is removed and a saline solution substituted.

An Investigation into the Ocular Changes in Normal and Hypertensive Pregnancy

By GRACE M. JONES, L.R.C.P., M.R.C.S., M.C.O.G.

THE lesions of the optic nerve and retina in pregnancy have been investigated fully by ophthalmologists, with whom the retinal picture, of necessity, assumes primary importance.

This investigation has been carried out entirely from the obstetrical standpoint, in the hope that it may be of value to the obstetrician who possesses only a very average knowledge of ophthalmology, but who with the aid of a standard ophthalmoscope can recognize any gross changes in the retinal picture. The appearance of the retina therefore has been noted in each case, and correlated with the general and renal condition of the mother.

The ocular changes in the present series of cases will be considered in two ways :—

- (1) The immediate significance of the changes, if any, with special reference to the termination of the existing pregnancy.
- (2) The prognostic significance as regards the future health and vision of the mother.

The conditions in the eye which are of interest are those for which some type of toxæmia of pregnancy is responsible, and those in association with hypertensive toxæmia have aroused the most discussion.

Various writers have endeavoured to show that different types of retinitis occur in different types of toxæmia, and that "albuminuric retinitis" is always diagnostic of chronic nephritis. Schiötz, Jean Corwin, and Herrick, among others, have shown, however, that retinitis can occur in any type of toxæmia in which hypertension is present. The differences described appear to be those of stage and degree rather than of type of retinitis.

Miller in 1915 stated "It has been my experience that the albuminuric retinitis of pregnancy affords evidence strongly indicative of primary nephritis, though it is not always present in cases of nephritic toxæmia".

Cheyney in 1924 stated that if a patient with toxæmia has retinitis the chances are 4:1 that she also has nephritis. He agrees with Schiötz, however, that retinitis does occur in acute toxæmia of pregnancy without evidence of pre-existing nephritis, and that a few of these patients do not show evidence of residual nephritis after the subsidence of the toxæmia.

These writers have stressed the œdema, exudate, and hæmorrhage which make up the picture of the retinitis. More recently greater importance has been paid to the retinal vessels. Mylius, in 1928, demonstrated that in toxæmia of pregnancy associated with a rise of blood-pressure, the most commonly observed lesions of the fundus were spasms and tonic constrictions of the retinal arteries. These occurred both in cases of acute toxæmia and in cases in which chronic nephritis had existed previously.

Wagener says that spastic lesions of the arterioles are the most frequent, and normally the primary, sign of retinal involvement in cases of pregnancy toxæmia. Hæmorrhage, œdema, and exudates occur secondarily to the arteriolar changes, as a result of interference with the nutrition of the retina. Wagener considers it justifiable to assume that the toxæmia of pregnancy, and also the presence of lesions in the retinal arterioles, are an indication of involvement of the systemic and renal arterioles, of similar type and severity, and that the development of retinitis indicates the approaching onset of organic injury to the retinal systemic and renal arterioles, which will be, in part, irreparable.

This is of particular significance with reference to the future well-being of the mother, since it is probable that hypertension will persist in the presence of diffuse generalized arteriosclerosis.

With regard to the termination of the pregnancy, Wagener considers that so long as the lesions in the arterioles are definitely spastic and the condition of the mother otherwise satisfactory, it is safe to wait. "Cotton-wool" patches and hæmorrhages indicate the approach of permanent organic change. Pregnancy should therefore be terminated to prevent the involvement of the renal arterioles, and the probable persistence after pregnancy of a low reserve or arteriosclerotic kidney.

He finds that spastic lesions occur in about 70% of cases of acute toxæmia. In about 60% of cases the spastic lesions disappear with the termination of the pregnancy, and the blood-pressure returns to normal, or to its previous level. In about 40% of cases organic lesions develop, often in association with retinitis. In such cases elevation of the blood-pressure usually persists.

Schiötz, Wagener, and Masters have followed up cases with retinitis occurring before and after the twenty-eighth week of pregnancy. A very large proportion of these have shown residual hypertension. The majority of these cases had no hypertension previous to pregnancy. It would appear, therefore, that if the integrity of the systemic arterioles is to be preserved, pregnancy should be terminated, if possible while the arteriolar lesions are still in the spastic phase, and certainly at the first indication of the onset of retinitis. Mussey, in a study of 108 cases of acute toxæmia, came to a similar conclusion.

Ocular signs and symptoms.—The most common symptoms are spots in front of the eyes, flashes of light, dimness of vision, distortion of images, and—occasionally—discomfort, but rarely pain. Very advanced retinitis may be present without complaint being made.

The ocular picture includes changes in the disc, retina, and vessels.

Apart from the spasm of the arterioles, swelling of the disc is the first change to be observed in the majority of cases. The disc is swollen, has indistinct margins, and is most often reddened. The swelling is largely due to œdema, and is nearly always accompanied by similar swelling of the adjacent parts of the retina. The whole fundus therefore tends to have a "steamy or hazy" appearance. If the process continues, white spots appear—cotton-wool or snow-bank areas. Most often these white patches are in proximity to the larger vessels, and the tendency is for the macula to be spared. Small white spots may later appear at the macula, usually in a linear arrangement, radiating from the fovea centralis, making up the stellate figure. Hæmorrhages are also commonly present from an early stage. They are frequently parallel and close to a large vessel. In long-standing cases of hypertension the arterioles may be narrowed and tortuous.

During this investigation very early changes have been frequently found—œdema of the disc and retina of varying degree. The changes in some cases have progressed and hæmorrhages and exudate have occurred. In other cases the fully developed picture of œdema, exudate, and hæmorrhage has been present on the first examination. Although most careful efforts have been made to recognize spasm and tonic constriction of the arterioles, the results have been disappointing. In many cases the arterioles have appeared to be a little narrowed, but it is difficult to determine whether they are abnormal. Spasm has only been recognized in about six cases. It is possible that in some cases the retinal picture had progressed too far, and that with much œdema the spasms are not so clearly seen. In general, however, it would appear that the condition is too difficult of interpretation for its recognition to be of any real value to the obstetrician, with his limited knowledge of eye conditions. Œdema of the disc and retina, exudate, and hæmorrhages, can certainly be recognized, and I will endeavour to show the significance of these lesions in the series of cases examined.

Method of investigation.—Ophthalmoscopic examination of the retina was made in 500 cases of normal pregnancy and 144 cases of hypertensive pregnancy. In the hypertensive cases the renal function was also investigated, and note made of the degree of hypertension.

Patients booked for the maternity home were examined in the ante-natal clinic on several occasions, but the majority of the toxic cases were admitted as emergencies, so that the retina could rarely be examined before admission.

Cases of normal pregnancy.—In the 500 cases of normal pregnancy examined at intervals throughout the pregnancy, no lesion of the fundus was found which could be correlated in any way with the pregnancy. The blood-pressure was low (110–130) in all cases.

Cases with hypertensive toxæmia.—These have been divided into three main groups, namely, cases with—

I. A systolic blood-pressure below 150 Hg; in this group there was usually only a small amount of albumin in the urine, and there was rarely any complaint of toxic symptoms such as headache, vomiting, or œdema.

II. A systolic blood-pressure above 150; in this group there was a moderate or large amount of albumin in the urine, and complaint of œdema, headache, &c.

III. Eclampsia.

The cases have also been graded in accordance with the amount of retinal involvement into four quite arbitrary grades:—

Grade 1: Mild œdema of the disc and retina.

Grade 2: Marked œdema of the disc and retina.

Grade 3: Small individual cotton-wool patches of exudate and hæmorrhagic areas in the retina.

Grade 4: Diffuse retinitis of the albuminuric type.

The findings in Groups I, II, III are best shown by a table which also indicates the amount of retinal involvement.

TABLE I.

Retinitis	Group I	Group II					Group III
	Grade 0	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	
Number of cases	34	35	17	26	5	7	19
Percentage of primiparæ	67	66	86	40	60	30	44
Average age	28	29	27	32	32	35	27
Number of days of toxic symptoms	9	13	17	24	30	39	17
Average highest blood-pressure	135/84	169/104	174/102	190/116	202/120	218/132	186/120
Percentage of average highest albumin	0.17	0.55	0.54	0.6	0.6	1.3	1.1
Percentage of deliveries 38–40 weeks	88	80	64	26	40	0	31
Percentage of deliveries 32–38 weeks	9	14	24	52	20	28	68
Percentage of deliveries below 32 weeks	3	6	12	15	40	62	11
Percentage of surgical inductions	0	20	29	50	40	85	47
Percentage of multiparæ with recurrent toxæmia	14	17	0	22	0	43	5
Percentage of primiparæ with history of renal disease	3	6	0	4	0	0	5
Percentage of children stillborn or dying shortly after birth	20	20	29	46	80	100	58

Eclampsia

Degree of retinal involvement

	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Number of cases (total 19)	5	4	4	6	0

All cases in Group I—that is, with a blood-pressure below 150 mm. Hg—showed a normal retinal picture.

In Group II, with severe hypertension, the degree of retinal involvement appeared to depend mainly on two factors—the height of the blood-pressure, and the duration

of the toxic symptoms. For example, the blood-pressure rose from 169 with a normal retina to 190 in retinitis graded 2, and to 218 in retinitis graded 4. In the same way an average of thirteen days of toxic symptoms was associated with a normal retina, and the duration of toxæmia increased proportionately with increasing retinal involvement, to thirty-nine days in retinitis graded 4. The amount of albumin appears to be of less account.

In the 19 cases with eclampsia, five had a normal retina, eight had slight oedema of the retina, and six had retinitis graded 3, that is, small patches of exudate and hæmorrhage. Considering the severity of the condition, the retinal involvement did not appear to be so marked as in cases of hypertension without convulsions.

The significance of the retinal involvement can be understood more readily if the result of a follow-up of cases is also taken into account. Of the 144 cases examined during pregnancy and delivery, 90 have been seen five months to two years after delivery. In the re-examination of the patients the renal function has been estimated by a urea concentration test, and a blood urea. Note has also been made of cardiac enlargement, accentuation of the aortic second sound, and complaint such as oedema and headache. No case is considered to have hypertension or nephritis without some definite evidence of renal or cardiovascular involvement. Thus patients with albumin in the urine alone, with good renal function and normal blood-pressure, have not been entered into the final figures as possibly having hypertension or nephritis. Therefore the figures obtained show a minimum percentage for each group. A further follow-up over a longer period may make the number returning with hypertension or nephritis even larger.

Table II differs little in essentials from Table I, but only the 90 patients followed up are included. The number and percentage of patients returning with chronic hypertension or nephritis in each group is shown.

TABLE II.

(Retinitis)	Group I	Group II					Group III
	Grade 0	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	
No. of cases ...	23	18	13	15	4	6	11
Percentage of primipare ...	63	66	84	33	50	33	54
Average age ...	27	29	27	33	32	35	28
No. of days of toxic symptoms ...	10	14	16	24	30	38	17
Average highest blood-pressure ...	135/85	164/102	174/101	192/117	201/120	217/131	185/115
Percentage of average highest albumin ...	0.15	0.5	0.56	0.61	0.6	1.2	1.0
Percentage of deliveries 38 to 40 weeks ...	82	88	54	33	25	0	27
Percentage of deliveries 32 to 38 weeks ...	9	6	30	53	25	17	63
Percentage of deliveries below 32 weeks ...	9	6	16	14	50	83	0
Percentage of surgical inductions ...	0	20	39	56	25	100	54
Percentage of multipare with recurrent toxæmia ...	21	17	0	31	0	50	9
Percentage of primipare with history of renal disease ...	0	11	0	7	0	0	9
Percentage of children stillborn or dying shortly after birth ...	21	17	30	53	75	100	54
Number of cases returning with hypertension or nephritis ...	0	3	2	5	2	5	2
Percentage of cases with hypertension or nephritis ...	0	16	16	33	50	83	18

Out of the 90 cases followed up, 19 developed chronic hypertension or nephritis—that is, 21%—which is in accordance with the findings of other investigators.

It can be seen that with increasing hypertension, and with increasing retinal involvement, the percentage of patients returning with chronic nephritis or hypertension also increases. The elevation of the blood-pressure is the result of general arteriolar constriction which may be due, according to Masters, to toxic substances circulating in the blood. If the toxic substance is not removed—that is, if pregnancy

is not terminated—permanent damage to the cardiovascular system results. Ultimately retinitis occurs with a prolongation of the toxic process. It would appear therefore that, considered in this way, the presence of retinitis is not always an indication of nephritic toxæmia as distinguished from pre-eclamptic toxæmia. The value of frequent ophthalmological examinations is evident. In patients under medical care, oedema of the disc and retina should be regarded with suspicion, and at the first sign of exudate or hæmorrhage pregnancy should be terminated. Diffuse retinitis should never be allowed to develop. Patients seen for the first time with a well-marked retinitis should have pregnancy terminated at once, with no attempt at medical treatment first. A delay of a few days may result in further injury to the arteriolar system, which may progress to irreparable organic changes.

If there is no previous history of renal trouble prompt intervention may arrest the general arteriolar changes, and normal renal function may be regained with a normal blood-pressure. If there is reason to suspect previous renal trouble, the retinitis is evidence of further arteriolar changes, which must also be arrested by termination of the pregnancy. Therefore from the obstetrical point of view, there is no difference in the treatment of any case with retinal involvement. Indicating, as it does, increasing arteriolar changes, the importance of termination of the pregnancy is the same in nephritic and pre-eclamptic toxæmia.

The indication for termination of pregnancy when toxæmia has progressed longer than fourteen days is shown in Table I. Prolongation of hypertension appears to be responsible for increasing retinal involvement, and with such involvement more patients are left with nephritic or cardiovascular lesions after delivery. Therefore if labour were induced 14–16 days after the onset of toxæmia the number returning with residual lesions would be considerably less. This would rarely mean the sacrifice of the child. The patients who tend to have living children are those in whom toxæmia begins late in pregnancy, so that induction would have little effect on the child. The more severe toxæmias frequently start earlier in pregnancy, often before or just when the child is viable. It will be seen in Table I that the fetal death-rate increases markedly with increase of severity of the toxæmia as evidenced by hypertension and retinal involvement. Therefore if the mortality is so high, there is little justification in attempting to tide the mother over for a few weeks in order to save the child.

The following case illustrates very well the onset of retinitis in pre-eclamptic toxæmia. A primigravida aged 26 was admitted in the twenty-eighth week of pregnancy. There was no history suggestive of any previous renal trouble, and she had not had scarlet fever. Before admission there had been oedema of the legs and face for two weeks, and headaches and spots in front of the eyes for one week. On examination, 0.3% of albumin was found in the urine and the blood-pressure was 174. There was oedema and congestion of the retina in each eye, and in the left eye two small hæmorrhages to the nasal side of the disc. Under treatment during the next week the general condition improved slightly, and the hæmorrhages in the left eye became almost completely absorbed. Five days later there was a very fine exudate along the vessels to be seen in each eye, and in view of this the membranes were ruptured to induce labour. Labour pains did not commence for six days after rupture of the membranes, and a living child weighing 2 lb. 7 oz., was delivered two days later—that is, twenty days after admission. During this time the blood-pressure increased to 190, the albumin had also increased, and there was slightly more exudate in the retina of each eye. Seven days after delivery there was a mass of exudate round the disc in each eye, passing along the vessels. The macula was clear, and the patient made no complaint of dimness of vision. Until the twelfth day of the puerperium the blood-pressure remained high, but on discharge on the nineteenth day it was 124. The retinitis was then showing signs of being absorbed. The child died shortly after birth.

On re-examination a year later there was no complaint of any renal symptoms, the blood-pressure was 110. There was only a very faint trace of albumin in the urine, and the urea concentration was 2.75%. On examination of the eyes, the exudate was seen to have been completely absorbed, but there were a few pigment changes at the macula. The vessels appeared normal.

This patient, so far as one can judge, was free from renal trouble previous to pregnancy. Therefore retinitis of the albuminuric type occurred with prolongation of the toxic process, and was not diagnostic of chronic nephritis. The hæmorrhages seen on admission should have been a sufficient danger signal for immediate induction of labour, but the fact that they became absorbed so rapidly seemed to show that the toxic condition was improving. As labour did not begin for a week after rupture of the membranes, there was a further period of hypertension which one had hoped to avoid. The case demonstrates the rapidity with which the retinal signs develop, and therefore the value of frequent ophthalmological examinations.

A similar type of case is in the wards now. The patient, a primigravida aged 29, was admitted when twenty-eight weeks pregnant, with a history of œdema and albuminuria for four weeks. There was no previous renal trouble. On the day of admission the blood-pressure was 190, and the eyes showed marked œdema of the disc and retina. The next day the blood-pressure had risen to 210, and there was a patch of exudate in the right eye to the temporal side of the disc. Labour was induced at once, and a stillborn child was delivered the next day. Three days after delivery, there was a further patch of exudate in the right eye, and a fine exudate in the left eye. Six days after delivery there was no further exudate, and the œdema and congestion of the disc was less. Possibly if this case had been treated expectantly in a hospital for a few days, a well-marked albuminuric retinitis would have developed. Induction of labour, with subsequent lowering of the blood-pressure, appeared to arrest the toxic process.

Five of the patients with retinitis of the albuminuric type were multiparæ and in two of these there was a history of previous toxic pregnancies, so that probably they had had nephritis or hypertension previous to the last pregnancy. One of these had a well-marked stellate figure at the macula in one eye. In all five cases there was definite cardiovascular or renal involvement on re-examination.

As far as vision is concerned, the prognosis in advanced retinitis appears to be reasonably good. In five of the cases the patients were almost blind—hardly able to recognize objects held in front of them. Even during the short stay in hospital the sight improved very rapidly, and on re-examination a year later, four had excellent vision. The fifth, who had a well-marked stellate figure at the macula in the left eye, had slightly impaired vision in that eye, but normal vision in the right. The fundi in each showed marked subsidence of the retinitis, although there were definite signs of changes still present. The vessels showed a little narrowing but otherwise appeared normal. The only case with marked sclerosis of the vessels was a primipara aged 29 who had had scarlet fever, but otherwise no apparent renal trouble. On admission, when she was twenty-one weeks pregnant, there was exudate in the eye, and marked tortuosity and sclerosis of the vessels, indicating long-standing changes. On re-examination the sclerosis was slightly more marked, the blood-pressure was 190, and there was thickening of the peripheral vessels. The renal function was considerably impaired, but in spite of these findings the patient said she felt in excellent health.

Although detachment of the retina occurs in severe toxæmia of pregnancy, no case was seen in the present series.

Conclusions

(1) Lesions of the retina must serve as a danger-signal, indicating that the patient has been allowed to continue in a toxic condition too long.

(2) In cases under medical care retinitis should never be allowed to develop; the first sign of exudate or hæmorrhage is an indication for immediate induction of labour.

(3) Patients seen for the first time with retinitis should have labour induced immediately.

(4) Patients having retinitis of the albuminuric type may have had previous renal disease, but retinitis may occur without any previous renal lesion if the toxic process is sufficiently prolonged.

(5) No case of severe toxæmia should be allowed to continue under medical treatment after fifteen days because, with persistence of toxæmia, the changes in the retina appear more frequently. There is no doubt that cases showing no ocular lesions have a much better remote prognosis as regards chronic nephritis or chronic hypertension.

(6) The prognosis as regards vision in cases with retinitis is reasonably good.

(7) Of the 90 cases re-examined 21% showed residual chronic nephritis or chronic hypertension. Of these, 1 : 7, with normal fundi—or with early retinal involvement—and 4 : 5 of those with advanced retinal involvement—showed residual lesions.

REFERENCES

- CHEYNEY (1924), *J.A.M.A.*, **83**, 1383.
 CORWIN, JEAN, and HERRICK, W. W. (1927), *Am. J. Obst. and Gynec.*, **14**, 783.
 MASTERS, R. J. (1933), *Tr. Am. Ophth. Soc.*, **31**, 416.
 MILLER (1915), *Am. J. Obst. and Gynec.*, **72**, 252.
 MUSSEY (1936), *Am. J. Obst. and Gynec.*, **31**, 938.
 MYLIUS, KARL (1928), "Funktionelle Veränderungen am Gefäßsystem der Netzhaut," Berlin, S. Karger.
 SCHIÖTZ, quoted by WAGENER.
 WAGENER, H. P. (1933), *J.A.M.A.*, **101**, 1380; (1934), *J.A.M.A.*, **103**, 1910.

DAME LOUISE MCILROY said that too little attention was paid by obstetricians to eye conditions in toxæmia. The presence of spasm of the arteries was an aid in the differential diagnosis between toxæmia and nephritis. Ophthalmoscopic examinations should be carried out in every case of nephritis in which induction of abortion was being contemplated. The prognosis of retinal changes was much more favourable in pregnancy than in any other condition, as even in cases of complete blindness, restoration of sight was not infrequently almost complete. The duration of the toxic condition was of more importance than its intensity.

Section of Otology

President—DOUGLAS GUTHRIE, M.D.

[May 7, 1937]

DISCUSSION ON OTITIS MEDIA IN EARLY CHILDHOOD (UNDER 5 YEARS)

Dr. J. M. Le Mée (Paris): *Oto-mastoiditis in infants*.—I use the term "oto-mastoiditis" because there is really no such thing as otitis media in the way in which we generally understand this expression, i.e. as meaning infection of the drum not involving the mastoid. Whereas in the child and the adult there are three compartments of the middle ear, in the infant there is only a single cavity extending from the pharynx to the mastoid. The Eustachian tube is short, and has a larger calibre than in the adult; the isthmus does not exist, therefore the contractions of the muscles of the soft palate have an action on the whole tube; the drum, ossicles, and membrana tympani are the same size as in the adult; the antrum is even larger, its external wall having a thin bone lamella.

Discussion on how the infection can reach and involve this passage would lead us too far, but when this does happen, the sequence is as follows: In the first stage the Eustachian tube is infected and the resultant "oto-salpingitis" is responsible for the fever and pain in the course of rhinopharyngeal infections. The drum is involved and reacts, as is shown by colour and aspect of the tympanum. On paracentesis, one has the impression of a bursting drum. No fluid is found at first but after from twenty-four to forty-eight hours it usually appears and at the same time the temperature falls and general conditions improve. Such facts may seem paradoxical since apparently the discharge seems to be due to the surgical intervention. It is indeed, merely a mechanical phenomenon; the opening of the tympanum allows the air to rush into the ear, just as when the peg of a barrel is removed. The contents of the Eustachian tube then flow out, the retention ceases, and the general trouble subsides; after a while everything is normal again.

The "primary purulent oto-mastoiditis" is a second type. It might resemble that of the child but for two facts. In the infant, the tympanum is reinforced by a myxomatous lining, and on the other hand, the Eustachian tube is wider; spontaneous perforation is therefore less frequent. This variety was described by André Bloch and ourselves under the so-called "latent otitis". I should prefer to call it "overlooked otitis" or "unsuspected otitis" because nothing draws the attention to the ear, the only symptoms being general or systemic. This type of otitis may be suspected: (1) In the presence of a febrile condition, the cause of which is not evident. (2) When, the cause of a febrile condition being known, the general phenomena persist in spite of the subsiding of the local signs (in bronchopneumonia, for instance). (3) When the treatment of a digestive condition only brings temporary relief. (4) Finally, whenever the infant seems to be in pain and, most important, presents persistent insomnia.

I will merely enumerate other better-known signs, such as: rolling of the head on the pillow; chewing; pain on swallowing; Pins' sign, or contralateral suction; alternating redness and pallor, Hallé's sign; pain on pressure over the canal, and certain

localized convulsions, especially ocular. In such cases the infant has a staring look ; from time to time, the eyeballs are turned upwards, showing a deviation either to one side, or in convergent strabismus ; this lasts so for a few seconds, and then there is a return to normal.

If the desired result is not attained after several paracenteses, we have to conclude that drainage through the drum is insufficient to clear the oto-mastoiditis and what might be called paracentesis of the antrum must be resorted to, but curetting is useless since only the mucous lining is infected.

The third type, less frequently encountered in the infant than in the child, is "osteitic oto-mastoiditis", clinically pictured by retro-auricular convexity. Antrum and cells (of which two groups often exist at birth—as Paul Bernard demonstrated radiologically—are separated from the tympanic cavity by obstruction of the aditus ; bone lesion is present, and the consequent suppuration, necrosis, and sometimes sequestration—keep up permanent infection. On opening, if the pus seems to be under high pressure, the diseased bone should be curetted, but if only muco-pus is found, one should be content with the curetting necessary for ensuring drainage, since, above all, surgery in infants should always be reduced to the minimum and operations should be as short as possible. In the Hôpital des Enfants Malades we, as a routine, first incise and rugine the periosteum. Two days later we open the mastoid. In such cases, X-rays are very helpful in the diagnosis.

The two other types of oto-mastoiditis cannot be put in the same group with those I have just described.

The type first reported in 1869 by Parrot, who, when carrying out autopsies of infants was surprised to note so often the presence of pus in the cavities of the middle ear—is really a post-mortem empyema, the cavities being only a reservoir for the pus produced in the nasopharynx. It is a principle of elementary physics that the cooling of the air contained in a cavity determines a fall of the pressure, resulting in this case in the penetration of the pharyngeal liquid into the middle ear. It is easy to verify, on the cadaver that the same principle applies to all other cavities in the cranium ; secretions will also be found in the two sinuses existing in the infant—i.e. the maxillary sinus and the ethmoid sinus. Why then is otitis always considered to be the cause of death, not sinusitis, which is just as serious a disease ? It is because, when doing an autopsy, one generally does not examine the sinuses. This precaution is also forgotten on examination of the living patient.

The type of oto-mastoiditis described as a cause of athrepsia is not really mastoiditis, and perhaps not even osteomyelitis, since it has been recognized by some authors that few polynuclears are found in these cases.

The reddish-yellow liquid which gushes out through the opening of the mastoid bone and which resembles pus, is also found in the sphenoidal body, in the occipital bone, in the sacrum, and in the sternum. Moreover, it may be found at the autopsy of non-athreptic patients.

In short, the presence of pus in the auricular cavities in the infant has not the same value and significance as in the child, and cannot be treated with standard procedures. In the pathology of the infant, the otologist should not content himself with otoscopy and X-ray findings ; he should use his own experience in interpreting the facts, and base his decision whether to operate or not on his general impression of the case, in collaboration with the pediatrician, rather than on strictly local signs.

Mr. T. Ritchie Rodger : I have analysed my case-records at the Victoria Hospital for Sick Children in Hull during the nine years since the Ear and Throat Department was instituted. There were 599 cases of otitis media occurring in children under the age of 3 years.

The large incidence of the bilateral infection is rather striking. Of the 599 cases, no less than 249 (i.e. 40%) were bilateral. The number of affected ears thus becomes 848. The distribution in the separate year-groups was as follows:—

Age	No. of cases	Single	Bilatera
Under 1 year	185	105	80 (= 40%)
1 to 2 years	200	114	86 (= 43%)
2 to 3 years	214	131	83 (= 38%)

The percentage of bilateral infection in the ages 3 to 4 was 36.5; in the ages 4 to 5 it was 20: so that it would seem that the high frequency of the bilateral condition belongs to the first four years of life.

This observation may be of some importance. In a great many cases the mother draws attention to one ear, which she has noticed to be discharging, or to which the baby seems to refer pain, as for example by constantly putting his hand to that side of the head. If we know that of all the cases brought to us probably 40% are bilateral or are destined to become so, we shall not make the mistake of omitting the examination of the other ear. Further, when we have found on our first examination that only one ear shows anything abnormal, we shall not omit to keep on examining the other ear at subsequent visits or while the patient is under observation in the ward. In a very large number of the cases in this series, the onset of the discharge, or the onset of symptoms demanding myringotomy in one ear was separated from that in the other by an interval of several days—sometimes even of two or three weeks. Occasionally we have not been aware of the imminence of discharge in the second ear. Even when one is watching quite carefully, the appearance of the membrane is sometimes non-committal, and the opportunity of giving relief by myringotomy is missed.

The incidence of mastoiditis requiring operation also proved to be higher than we had expected.

For cases under 1 year it was 19% of all affected ears.			
" " 1 to 2 years	" 26%	" " "	" "
" " 2 to 3	" 26%	" " "	" "
" " 3 to 4	" 21%	" " "	" "
" " 4 to 5	" 21%	" " "	" "

In this matter, of course, the personal views of the surgeon come into play. He has no control over the number of cases of otitis media which occur, whether unilateral or bilateral, but the number of cases subjected to operation is to some extent determined by his individual view. Possibly some surgeons would have had a larger proportion of operations in this series, others possibly a smaller. One of the chief aims we set before ourselves is the prevention of chronic otitis. We try to keep every case under observation and carefully treated, until the ear is quite dry. If conservative treatment—including, in a large proportion of cases, the removal of adenoids—is not successful in a reasonable time, we assume that the discharge is being fed from the mastoid antrum and we recommend operation. The "reasonable time" varies with the individual case. If, for instance, the discharge is diminishing gradually and the general condition is good, we are content to wait longer; on the other hand, if the child continues to look seedy and the discharge remains profuse, three or four weeks is long enough to wait, even with a normal temperature and no mastoid signs. In the presence of continued mastoid tenderness or continued temperature we, as a rule, do not wait at all. Working on these lines we find only very rarely that we have to enter on the case record that operation might have been postponed or avoided, but it is better to run the risk of a mistake of this kind occasionally, than to follow any rule which might swell the ranks of the chronic otorrhoeas.

A further point may be worth noting. It does not appear that the fact of an infection being bilateral indicates an increased virulence. The percentage of mastoid operations among these is not greater than in the series taken as a whole.

In the 80 bilateral cases under 1 year there were 9 bilateral Schwartz operations and 7 single.			
" " 86 " " 1 to 2 years	" 19	" " "	" 7 "
" " 83 " " 2 to 3	" 20	" " "	" 12 "

The association of otitis media with diarrhoea-and-vomiting has been a fairly frequent occurrence. Quite frequently also we have had to ask the help of one of the physicians in determining whether the temperature and other constitutional signs were likely to be attributable to a coincident chest condition rather than to the ear. We have generally put it to him that if he cannot say there is sufficient in the way of pulmonary signs to explain the temperature and malaise, we would propose, with his consent, to explore the mastoid. These are the only cases in which we aim at speed in operating—out of deference to the chest condition.

The incidence of tuberculosis has proved surprisingly small. Members of the Section are acquainted with the figures presented by Dr. Logan Turner and the late J. S. Fraser, when the subject of tuberculosis of the middle-ear cleft was discussed in 1914.¹ Of the cases of otitis media seen in the Ear and Throat Department of Edinburgh Royal Infirmary during the eight years prior to 1914, 50% of those under 1 year, and 27% of those in the second year of life, were judged to be tuberculous—after pathological examination in about half the cases and on the basis of unequivocal signs in the others. In the hospital from which my figures are taken we have made it our practice to send material from the mastoid operation only in those cases in which tuberculosis was at all suggested by the appearances or signs. Even so, a negative report has been much more frequent than a positive one and when I say that my colleague, Mr. R. R. Simpson, agrees with my impression that not one case in ten has aroused our suspicions, it follows that our estimate of the incidence is something less than 5%.

When I began this analysis a few months ago, we arranged that in every case of mastoid operation on a patient under 3 years of age, bone tissue and pus should be sent for examination. The number is too small to be of value by itself, but it was the best we could do in the time and the result bears out the above estimate. Of 14 cases, only one was reported to be positive, and that was in a child of 2½ years who had no history of otitis before three months previously. One-in-fourteen is a little more than 5%, but on the other hand the first and second years—which are the years of the high incidence in Dr. Logan Turner's cases—gave a nil percentage for 13 cases.

In the paper referred to, Dr. Turner waged war against the insanitary condition of the milk supply in Edinburgh and the surrounding area. He quoted researches by Mitchell and John Fraser on tuberculous gland and tuberculous bone conditions respectively, and referred to their conclusions that in 90% of the gland cases and 60% of the bone cases, the bovine type of the tubercle bacillus was proved to be the causative factor. He assumed that in middle-ear tuberculosis the same type of organism is active and that the mode of infection is by the regurgitation of infected milk into the Eustachian tube. In the subsequent discussion all the speakers agreed with this view as to the source and route of infection. Mr. Fraser, in replying to the discussion, as reported in the *Proceedings*, concluded with these words,

"If all tuberculous cows were slaughtered, following a tuberculin test, there would be little or no need for operation on tuberculous otitis media, as the cause would have been eliminated."

If, then, we could accept these two sets of figures—the Edinburgh figures of 1914 and mine of 1937—as exactly comparable, we might claim that within a quarter of a century improvements in sanitation and particularly in the milk supply had achieved all that Fraser in these words had adumbrated—and more than has been achieved probably in the case of any other form of tuberculosis.

There are, however, fallacies in the comparison. In the first place we are comparing conditions in two different cities, whose incidence of tuberculosis in general and of middle-ear tuberculosis in particular may not have been the same in 1914 and may not be the same to-day. I think it was accepted in 1914 that the incidence of tuberculosis in Edinburgh was much higher than in most English towns and cities.

¹ *Proc. Roy. Soc. Med.*, 1914, 3 (Otol. Sect., 15).

Secondly, we have to remember that the *percentage* of tuberculous cases in a series can be lowered quite as well by an increase of the non-tuberculous cases as by a diminution of the tuberculous—and there is no doubt whatever that this has occurred. With increased knowledge, on the part of both parent and practitioner, of the importance of early attention to ear conditions, with child-welfare workers and home nurses and other officials literally hounding the cases to our special clinics, we see, especially in hospitals for children, large numbers of cases of the milder and more transitory type of otitis, such as a generation ago never reached the specialist. Very many of the cases in my series attended within a day or two after the first symptoms began—many others were already on the way to spontaneous cure when first seen. My recollection of working with Turner and Fraser in 1914 is that we saw a comparatively small number of such cases. The persistent ones, on the other hand, including all the tuberculous cases, were sure to turn up sooner or later. It may even be the case that the non-tuberculous otitis media not only escapes our attentions less frequently nowadays, but is actually more common. Influenza comes upon us in successive waves. The *Streptococcus haemolyticus* seems to be always with us.

Still, the difference between 50% and 5% is large enough to allow for a generous discount on all these points, while still leaving us with the comforting impression that we have witnessed in our own generation a very great diminution in the incidence of tuberculous otitis. If this is true, we have to accommodate our outlook and our treatment to the altered facts. It was emphasized by Fraser in 1914, and is generally agreed, that the treatment for tuberculous otitis must be radical. If we hold an exaggerated idea of the frequency of the condition, we shall be inclined to sacrifice the hearing in many cases in which a simple Schwartze operation would give a completely successful result, and save the hearing.

Dr. J. H. Ebbs: I would like to focus attention upon the incidence of acute otitis media, particularly in children suffering from conditions associated with it, or resulting from it. Perhaps the best way to approach the problem from an otological, as well as a pathological and pediatric, aspect, will be to show an analysis of the results of the post-mortem examination of the middle ear and mastoid region in 880 children varying in age from birth to 14 years. These children have died from a great variety of medical and surgical conditions. The records appear to be of value, since they are those of consecutive examinations of almost 100% of the children who have died in a children's hospital which receives its patients from a large area in the Midlands. These examinations were begun by my predecessor and senior, the late Dr. R. J. Gittins, and were carried on soon after their commencement by myself and those who have been connected with my department.

During a period of about four years, 880 children have been examined post mortem, to determine the presence or absence of infection of the middle ears and mastoid regions. Infection has been recorded as present only when actual purulent material has been found. Serous fluid, clear gelatinous material, and other fluid which was not composed of pus cells have not been recorded as purulent. Of the 880 examinations made, purulent material was found in one or both ears in 52.8%. In other words, more than one half of the children who have died in this hospital have been found to have a purulent infection in the middle ears and mastoids. A study of Table I shows that 70% of these children were under 1 year of age, 80% were under 2 years, and almost 90% were under 5 years. Infants under 1 year provide only about one-third of the total admissions to the hospital, and yet this age-group is responsible for 70% of the deaths. This, I believe, indicates clearly the age-group in which the mortality rate is a serious one. A glance at Table II indicates the strong possibility that otology might help in attacking this death-rate in infants, since it shows that 61% or 368 children out of 603 under 1 year had purulent otitis media when they died. Of children dying during the second year of life, 52% were found

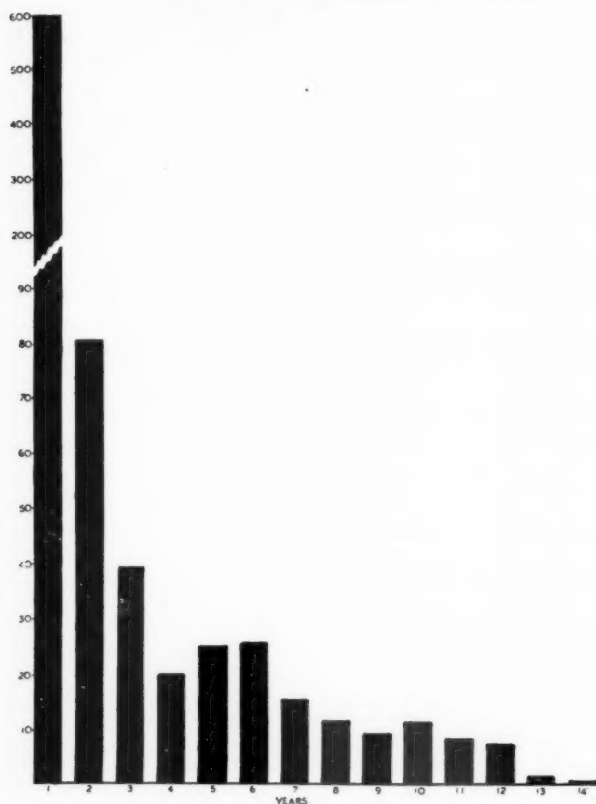


TABLE I.—Age distribution of children examined at autopsy for the presence of otitis media.

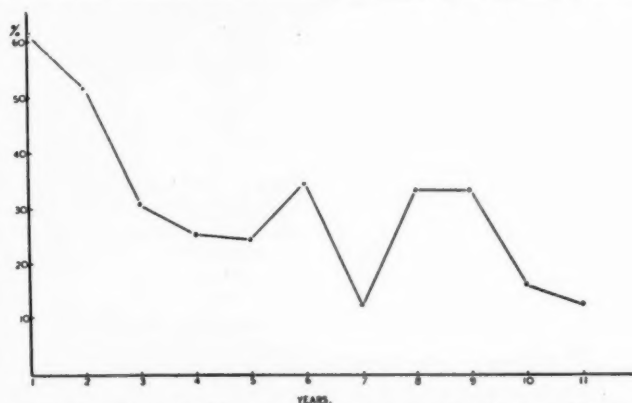


TABLE II.—Percentage of children in different age-groups found to have otitis media.

to have otitis media, while of those dying in the other years 30% or less had the condition. The peak in the curve between 5 and 6 years might be attributed to increased incidence when the child first goes to school. Perhaps percentages are misleading, with such small numbers, in the older age-groups, but Table III shows the actual number of cases. Those with infection are indicated in black columns, and those normal in the white columns.

The number found to have otitis media in the first year of life, as well as the total number examined, is so large in proportion to the other years, that in trying to illustrate them graphically the columns extend far beyond the limits of the graphs. For this reason, I have analysed the records of the first year and set them out for the

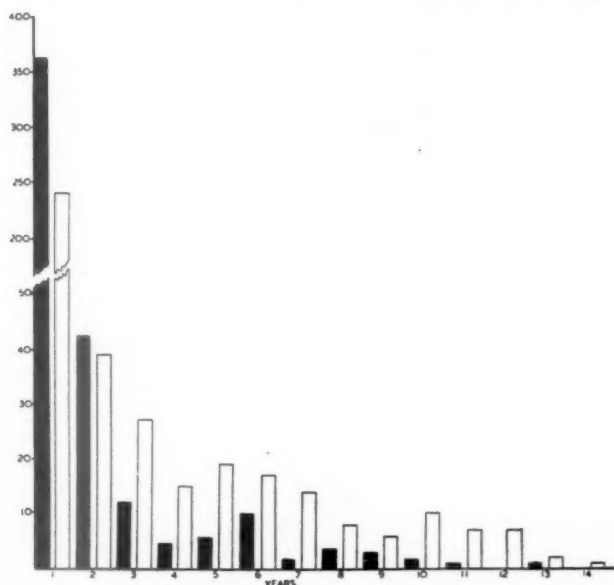


TABLE III.—Number of children found at autopsy to have otitis media indicated in black columns, those without otitis media in white columns.

different months. Thus in Table IV it will be seen that the number of infants dying in the first few months of life rapidly decreases, while the incidence of otitis media rapidly increases up to the age of 3 months, when it remains more or less about 70% throughout the remaining month periods of the first year (Table V).

The rise to 90% at ten months is based upon only 20 cases in this age-group, and therefore its significance is open to question (Table VI). Of 120 infants dying during the first month of life, 38 had otitis media and in one of these it had occurred in the first week of life, illustrating the early age at which infection is possible.

A general survey of these charts has brought me to certain conclusions. The incidence of otitis media found, at autopsy, in all infants and children dying in a large children's hospital, is extremely high in those dying during the first year of life, and the incidence decreases as the older age-groups are reached. The incidence of otitis media increases rapidly from birth, when it is not found, until the age of 3 months, and then remains almost constant through the first year of life.

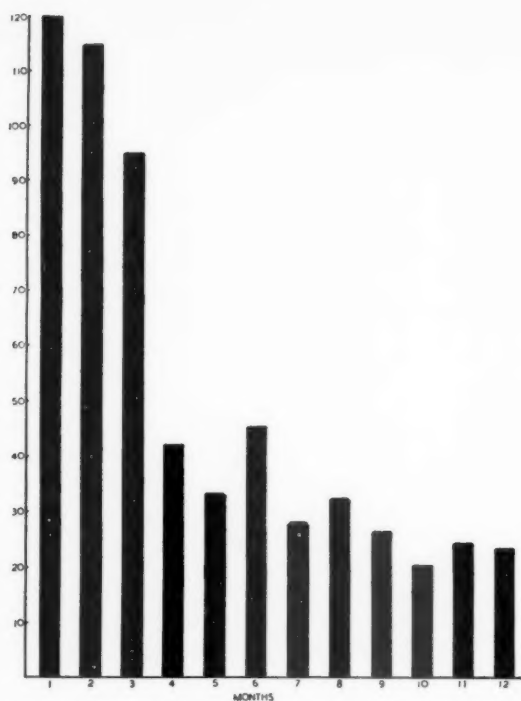


TABLE IV.—Age distribution in months, of infants examined at autopsy who have died during the first year of life.

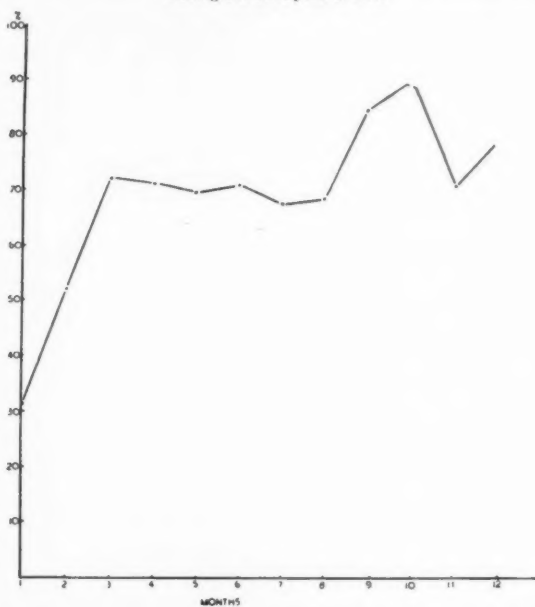


TABLE V.—Percentage of infants in months of first year found to have otitis media.

Perhaps it would be as well to state that I am not implying that those found with otitis media at autopsy have necessarily died as a direct result of this condition. I can only say that purulent infection was present macroscopically; this was confirmed in a large number of cases by microscopical examination of the pus. No attempt has yet been made to study the histological changes in the mucosa and bone of this region. We hope to complete this at some future time.

Associated sinusitis.—While this discussion is confined to otitis media, it might be of interest, in passing, to mention a similar study which has been going on at the

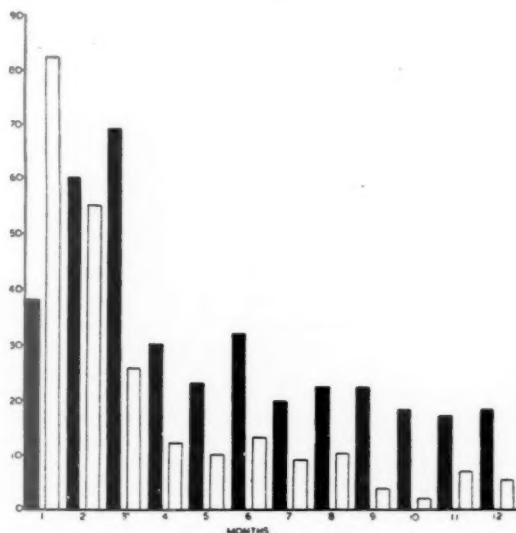


TABLE VI.—Number of infants found at autopsy to have otitis media indicated in black columns; those without otitis media in white columns.

same time, in an attempt to determine the incidence of sinusitis in infancy and childhood. There is not time, nor is this the place, to analyse the figures in detail, but the association of sinusitis and otitis media is illustrated by the fact that of 496 children in whom one or more of the accessory nasal sinuses were examined, purulent infection was found in 152, or 30.6%.

Table VII shows that while 33 had purulent infection of the sinuses without an

TABLE VII.—THE RELATION OF OTITIS MEDIA TO SINUSITIS.

Sinuses.			
Total number examined, 496.			
One or more sinus infected	152 (30.6%)
Otitis media with associated sinusitis	119 (24.2%)
Otitis media without associated sinusitis	161 (57.5%)

associated otitis media, 119 had sinusitis associated with otitis media. In other words, of 496 children of all ages, otitis media was found in 280 or 56.4%, sinusitis in 152 or 30.6%, and both together in 119 (24%). 42.5% of the 280 children with otitis media also had sinusitis.

A recent article by Crooks (1937), from the Hospital for Sick Children, Great Ormond Street, revealed the fact that 24% of 100 children whose antra were examined were infected. These were children in the older age-group, who were having tonsils and adenoids removed. This important clinical study of the disease illustrates the frequency of the condition. Crooks (1937) found that 44 of 100 children examined for sinusitis had otitis media. In this post-mortem series 56.4% had otitis media.

Bacteriology.—A bacteriological study of the pus found in the ears and sinuses at post-mortem in 200 cases is shown in Table VIII. The streptococcus was found

TABLE VIII.—THE INCIDENCE OF VARIOUS ORGANISMS FOUND IN 200 CASES OF OTITIS MEDIA.

Total number of organisms found, 275.

<i>Streptococcus</i> ...	139	(50.5%)
<i>Pneumococcus</i> ...	49	(17.8%)
<i>Staphylococcus aureus</i> ...	35	(12.7%)
<i>Staphylococcus albus</i> ...	24	(8.7%)
<i>H. influenza</i> (Pfeiffer) ...	15	(5.4%)
<i>Meningococcus</i> ...	4	(1.4%)
<i>Micrococcus catarrhalis</i> ...	3	(1.0%)
<i>B. coli</i> ...	3	(1.0%)
<i>Tubercle bacilli</i> ...	2	(0.9%)
<i>Diphtheria bacillus</i> ...	1	(0.3%)

in 50%, the pneumococcus being next in frequency, followed by staphylococcus and Pfeiffer's bacillus. It is interesting to note that the meningococcus was found in the ears in four cases of cerebrospinal fever with mastoiditis. The tubercle bacillus was identified in the middle ears in two cases of tuberculous meningitis, and the diphtheria bacillus in one child with otitis media. No attempt has been made to classify the types of the different organisms for the purpose of this communication.

Now I should like to review these statistics from a pediatric point of view, trying to assess the principal causes of death in the group of children studied.

Associated gastro-intestinal disturbances.—The pediatrician devotes a large part of his time and study to the problems of nutrition in infancy and seems to have arrived at what may be described as almost an optimum understanding of nutrition in the normal infant. But it is in certain nutritional disorders of infancy which are associated with infections, that difficulties continue to be a problem. As Marriott (1927) has said, "Otitis media is the most frequent infection responsible for nutritional disturbance". With this in mind, an analysis of these 880 case records revealed the fact that 238 children under the age of 2 years suffered from gastro-enteritis, characterized by diarrhoea-and-vomiting, which was either the major complaint or was a complicating factor in the cause of death. Table IX shows that 193 or 81.4% of these

TABLE IX.—THE INCIDENCE OF INFECTIONS IN GASTRO-ENTERITIS (238 CASES).

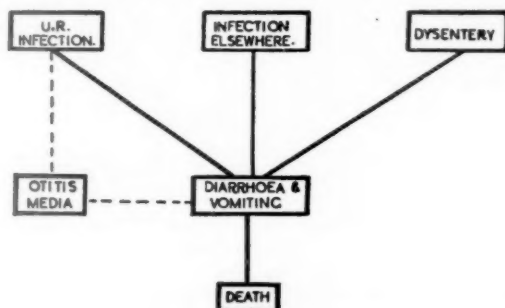
With otitis media ...	193	(81.4%)	} 91.6%
With other infections ...	25		
Without demonstrable infection ...	20		

cases had purulent otitis media, 25 had a parenteral infection elsewhere, while only 20 showed no evidence of infection. In other words, 91.6% had an associated parenteral infection, which in most cases was an otitis media. I realize that such statements put me on precarious ground, and yet the importance of the question tempts me to enlarge upon this particular condition, keeping the above figures in mind.

Diarrhoea-and-vomiting is described under a variety of terms, such as gastro-enteritis, cholera infantum, intestinal intoxication, dyspepsia, &c. It is a condition which has been studied for many years by many investigators and, as a result, various aetiological factors have been put forward. Some of the early investigators found the

dysentery bacillus and considered it to be the undoubted cause. Another early idea was revived by Floyd (1925), Jeans (1926), Marriott (1927), and others, who considered that gastro-intestinal disturbances were related to otitis media. The streptococcus seems to have been the organism found most frequently in the otitis media associated with their cases.

An investigation of summer diarrhoea has been carried on for some years in the Hospital for Sick Children in Toronto, under the direction of Dr. Alan Brown (1930). This investigation has proved that a large number of cases which occurred in summer epidemics were due to dysentery organisms, several different organisms being present. *B. dysenteriae* Sonne was found fairly frequently in the above series. Otitis media was found in 44 of 171 cases of intestinal intoxication examined upon admission to the above Hospital, while 65 other children developed otitis media during the course of their illness. A total of 109 cases (63.7%) of diarrhoea had otitis media. The Toronto investigators also found that 63.1% of 84 control cases had otitis media, and there was a higher percentage of streptococcus in these than in the cases with diarrhoea.



They came to the definite conclusion that neither otitis media nor the streptococcus was responsible for the diarrhoea-vomiting syndrome. I was fortunate enough to be able to observe and take a small part in the above study, and I must confess that the results were most convincing.

After seeing hundreds of cases of diarrhoea-and-vomiting, I recognize a classification which includes the ætiological factors mentioned above. Carmack (1930) has described a similar classification. I am convinced that they can be divided into three groups, the largest consisting of those cases of diarrhoea and vomiting which are secondary to an upper respiratory infection. This infection might be so slight as to be unrecognized in a young infant. Otitis media usually becomes evident in this group, either at the onset or at a later time, but it is not necessarily present. The second group is also a large one, being those cases beginning with one of a great variety of parenteral infections which develop the diarrhoea-vomiting syndrome during the course of the illness, and sometimes as a terminal event. Examples in this group are pneumonia, abscesses, erysipelas, &c. The third group, and in my experience here, the smallest, is that of cases due to a definite enteric infection, in other words true dysentery. In a large series of stool cultures made in this series, pathogenic organisms were found in only four cases, and two of these were the result of a known epidemic of Sonne dysentery. Blood and mucus are often found in this last group.

It must be remembered that I am quoting post-mortem figures; nevertheless they support my impressions from observations of a large number of clinical cases. The above classification recognizes both an enteric infection group and also a parenteral-infection, or secondary, group. The ætiological factor in the latter group is, in the

majority of cases, an infection somewhere in the respiratory tract. I do not consider that the infection is confined to the middle ear and mastoid antrum, as some have tried to show. An infection anywhere in the body of an infant with low powers of resistance is capable of producing the diarrhoea-vomiting syndrome. While otitis media may not in every case be the initiating cause of this condition, it may develop during the course of it, and the toxic effects of a mastoiditis may not only prolong the diarrhoea but be the factor which determines the fatal outcome of the illness.

I am often asked, particularly by new Residents, how they are to diagnose otitis media, mastoiditis, and sinusitis—which I almost invariably find at autopsy—in infants with gastro-enteritis. They tell me that it is simple in those cases which show classical signs and symptoms—such as fever, vomiting, and a red, bulging ear-drum which produces a rapid discharge when a paracentesis is performed, followed by a marked clinical improvement—but unfortunately, these cases are few. The more common finding is either a dull red, or a grey, lustreless, drum, which often shows no bulging and when incised is boggy, and may or may not produce any discharge. So often, the drums are incised and no pus is found, yet at autopsy the mastoid region is full of thick pus, the whole area showing evidence of marked infection, which obviously was present for some time before death. It is interesting that in some cases of suspected otitis media in which pus does not appear on paracentesis, the ear will begin to discharge profusely when the dehydrated infant has had its fluid balance restored. The temperature charts vary greatly in this condition, as indeed they do in many conditions of infancy. High temperature is associated with acute signs and symptoms of the otitis media, but most cases of the diarrhoea-vomiting syndrome show a low-grade irregular temperature, about 99°–100° F., or else a normal, or even subnormal, temperature. It is perhaps unreasonable to expect anyone to diagnose otitis media in an infant who has a subnormal temperature, normal-appearing drums, and who shows none of the signs of otitis media. This occurs very frequently in dehydrated infants who are premature, marasmic, or failing to thrive. I have observed that often such infants will show the presence of their infection by a distinct rise in the pulse-rate from that at which it has been maintained previously. In many such cases there is not any alteration of the temperature.

From these latter remarks it will be seen how difficult it is to mention treatment of such conditions. Dean and others have advocated the drainage of the mastoid antrum, believing that otitis media is a large factor in this disease. Simple cortical mastoidectomy has been performed in several centres. Carmack (1930) has reported 30 cases of diarrhoea-and-vomiting, in which mastoidectomy was performed; 22 recovered and 8 died. Wishart (1930) in Toronto performed the operation in a number of cases but came to the conclusion that it was not helpful. Only a few mastoidectomies have been attempted in our hospital, and those only for patients who have been extremely ill—in fact, almost beyond hope—so that the results have not been very successful. Carmack (1930) seems to have the most rational attitude towards the problem of mastoidectomy when he says that—

“Surgical intervention cannot be decided upon intelligently without close co-operation between the pediatrician, the otologist and the radiologist. No mastoid should be opened without clinical evidence of disease in the mastoid space. Adequate pre-operative and post-operative treatment is of vital importance. All infants with marked or continued gastro-intestinal disturbances should have careful ear examinations, and if pathology is found, early and free drum incision should be made. If the mastoid is involved and satisfactory improvement is not had by ear drainage, a mastoid operation is indicated. Operation, except in the occasional case, should not be attempted during the violent gastro-intestinal crisis.”

I might add to this that in my opinion indiscriminate operations upon the mastoid antrum in infants with acute gastro-enteritis would be as disastrous as if no form of treatment were instituted. Simple paracentesis should be the first step, followed,

if found necessary, by simple drainage of the mastoid antrum. When there are definite indications present this latter procedure should not be reserved until the infant is almost moribund, nor should it be undertaken unless the infant has been prepared for operation, to the satisfaction of the pediatrician.

Pneumonia.—The post-mortem finding of pneumonia in children is so common that it often becomes difficult for the pathologist to assess its importance in the consideration of the primary cause of death. Sometimes the information which is available is too scanty for an accurate decision to be made on this point. However, in analysing these records, I have attempted to divide pneumonia into two groups. One group I have called "primary," and this includes all cases admitted to hospital with a confirmed diagnosis of pneumonia which has appeared to be the most important initial condition. The other group is called "secondary" in the sense that all these children have been admitted to the hospital with some other important condition, but have had an associated pneumonia, or have been found to have pneumonia at autopsy. A survey of Table X shows that 71.6% of 134 so-called "primary"

TABLE X.—THE INCIDENCE OF OTITIS MEDIA AND THE INCIDENCE IN PNEUMONIA.

Age Years	Primary Disease		Secondary to Other Disease		Totals	
	Otitis Media	Normal	Otitis Media	Normal	Otitis Media	Normal
1 ...	71 (80.7%)	17	130 (70%)	55	201 (75.3%)	72
2 ...	10 (71.4%)	4	14 (70%)	6	24 (70.7%)	10
3 ...	3 (60%)	2	3 (60%)	2	6 (60%)	4
4 ...	1 (20%)	4	3 (60%)	2	4 (40%)	6
5 ...	4 (57%)	3	3 (75%)	1	7 (60%)	4
6 ...	2 (28.5%)	5	2 (66%)	1	4 (40%)	6
7 ...	2 (66%)	1	2 (100%)	0	4 (80%)	1
8 ...	1	0	3	0	4 (100%)	0
9 ...	2	1	0	0	2	1
10 ...	0	0	0	0	0	0
11 ...	0	0	0	0	0	0
12 ...	0	1	0	1	0	2
Totals	96 (71.6%)	38	160 (70.2%)	68	256 (71%)	106
	134		228		362	

pneumonias had an associated otitis media at autopsy, while 70% of 229 "secondary" pneumonias also had otitis media. It will be seen that pneumonia was an even more frequent finding than gastro-enteritis in these children, and once again the enormous number in the first year of life is quite appalling. Of these children 71% were found to have infected middle ears at autopsy. What is the significance of this? Campbell (1934) studied 130 patients with pneumonia, most of them young children, and he found that 70% of them had otitis media, while 100% had sinusitis. He suggested that sinusitis was a possible aetiological factor in the production of pneumonia. Cullom (1934) expressed the opinion that infection of the upper respiratory tract is a "menace to all lower lying structures". Thus it may lead to tonsillitis, bronchitis, bronchiectasis, pneumonia, and severe gastro-intestinal disturbances. Whether otitis media or mastoiditis is a significant factor in the aetiology of pneumonia or not, it is apparent to me that the high percentage of children who die with pneumonia and have an infection of the ear, is very strong evidence in favour of a preceding, concurrent, or secondary upper respiratory infection. The fact that nearly all of these children were found to have bronchopneumonia rather than lobar pneumonia is further evidence of it being secondary to, or associated with, upper respiratory infection.

Before going on to other diseases and the association of otitis media with them, I should like to mention one or two explanations which have been given for the presence of pus in the middle ears as found at autopsy. It has been said that any infant or child who is suffering from a chronic or lingering, debilitating illness will have a collection of fluid in the middle ear. In other words, it is the result of a terminal

infection. This is an explanation which Lierle (1927) discusses and which he names an "agonal event".

The second explanation is that the pus is of an exogenous nature—i.e. that the condition is not a true otitis media but an empyema of the middle ear, which is a supplementary reservoir for the pus from the nasopharynx. If such were the case one would expect to find milk and other fluids draining into the middle ear. None was found in any of the cases examined in this series.

The third and I believe the most logical explanation is that pus found in the ears post mortem is the result of an otitis media which has developed before the onset, or during the course of, the principal disease which led to death. I believe that the otitis media has been an initiating cause in a great many of the diseases found in these children. That the pus found at autopsy is not due to the child lying in a semi-conscious, debilitated state is borne out by a study of Table XI, which lists a number

TABLE XI.—THE LOWER INCIDENCE OF OTITIS MEDIA IN THE UPPER GROUP OF DISEASES ILLUSTRATED.

Diagnosis	Otitis media	Normal
Rheumatic carditis	0	15
Brain tumour	2	7
Appendicitis	1	8
Intussusception... ..	1	11
Leukemia	0	5
Bacterial endocarditis	0	4
T. B. meningitis	17	44
Cerebral sinus thrombosis	17	0
Brain abscess	4	0
Hare-lip and cleft palate	11	0
Pink disease	16	1
Meningitis	58	18

of illnesses showing a very low incidence of otitis media, in spite of the fact that some of them are conditions which go on for a considerable time before the child finally dies. Thus rheumatic carditis showed no evidence of infection in the upper respiratory tract in 15 cases examined. Nine cases of brain tumour were examined and only two had otitis media—but on the other hand in four cases of brain abscess there was gross infection of the ears and sinuses. Appendicitis with general peritonitis, and intussusception are conditions with shorter courses but they also show little evidence of infection in the middle ears. There was no infection in four cases of bacterial endocarditis, and only 17 out of 61 cases of tuberculous meningitis had suppurative otitis media. The tubercle bacillus and tuberculous granulation tissue were found in one of the latter. Everyone is familiar with the lingering semi-conscious or unconscious state in which these children lie for many days before their death. If otitis media occurred as an agonal event then I think it only logical to expect a much higher percentage of cases dying from the above conditions, to have otitis media at autopsy.

In the second part of Table XI are listed a few conditions in which otitis media was invariably found and was probably of considerable importance as a factor in the cause of death. Seventeen patients, varying in age from a few months to several years, died of cerebral sinus thrombosis. I have recently made a detailed study of these cases, which have been reported elsewhere, and in every case I have found evidence of an upper respiratory infection. After considering various theories as to the possible cause of this condition, I have come to the conclusion that the majority are the result of infection in the nasopharynx. I am referring here not only to those cases which involve only the lateral sinus in the presence of mastoiditis, but also to those with thrombosis of other sinuses—particularly the superior longitudinal sinus. I think that it is safe to say that nearly every child with hare-lip and cleft palate develops otitis media and sinusitis at some time during its early life. A defective lip, palate—and, often, nose—predispose and encourage the entrance of infection

to the accessory air passages. It is therefore not surprising that the 11 children who died—having this malformation—were infected.

Pink disease, that curious malady of infants and young children, the ætiology of which is still obscure, makes the child a notoriously poor risk in the presence of infection. In fact, children with this disease are so susceptible to infection that many pediatricians avoid admitting them to the general wards of a children's hospital. They do not all die, but in even the best circumstances the mortality is high, and it is interesting to note that those who have died in our hospital have, with one exception, had otitis media.

The diseases listed in the upper half of Table XI, showing a relative freedom from otitis media, are in sharp contrast to those in the lower half of the table, where otitis media is almost the rule. These figures are, I believe, very strong evidence that otitis media is of considerable importance in the group of fatal illnesses.

Associated meningitis.—Meningitis was the principal cause of death in 137 of this group of 880 children. Excluding the 61 cases of tuberculous meningitis mentioned above, there were 76 children with a purulent meningitis (Table XII). In

TABLE XII.—THE ASSOCIATION OF OTITIS MEDIA WITH PURULENT MENINGITIS.

	Otitis Media	Normal
Meningococcal	12 (60%)	8
Streptococcal	22 (95%)	1
Pneumococcal	10 (71%)	4
Influenzal	7 (87.5%)	1
<i>B. coli</i>	6 (60%)	4
Staphylococcus	1	0
	58 (76.3%)	18

meningococcal meningitis 12 had otitis media at autopsy and eight were normal. As mentioned before, the pus from the ears of four cases grew the meningococcus when cultured. It is difficult to say that the organism in the ears had any relation to the meningitis, other than that of infection of the nasopharynx, which is recognized as the first stage of the disease. These findings however, suggest that we should examine every case of cerebrospinal fever very carefully from an otological point of view, in order to discover otitis media when present, and treat it as indicated. I cannot help feeling that such a focus of meningococcal infection might have been the deciding factor in the fatal result in some of these cases. Careful cultures for the meningococcus should be made in all cases of cerebrospinal fever with otitis media and treatment with serum should be continued as long as infections are found either in the cerebrospinal fluid or in the ears.

Streptococcal meningitis occurs most frequently as a complication of mastoiditis. It is a condition which is familiar to every ear, nose, and throat surgeon. Twenty-three children in this group have died from streptococcal meningitis, which in 22 cases was secondary to mastoiditis and in one, was a complication of a general streptococcal septicæmia. These figures are very common experience and therefore do not require any further comment.

Out of fourteen cases of pneumococcal meningitis an upper respiratory infection was found in all but two. In 10 of these there was otitis media, while one case followed removal of tonsils and adenoids. The remaining child had a purulent pneumococcal infection of the sinuses. Seven of the eight cases of influenzal meningitis had an otitis media. Meningitis due to *Bacillus coli* was in each case secondary to spina bifida, while the one caused by staphylococcus was the result of osteomyelitis.

Prophylaxis.—Leaving this appalling list of morbid figures, I will briefly mention one or two points which offer slight hope of reducing the mortality in some of these diseases. Beginning at birth, the first form of prophylaxis is breast-feeding. An analysis of the notes which I have made on all the infants in this large series, reveals

the startling fact that of those dying of infections related to otitis media and sinusitis—especially gastro-enteritis and pneumonia—only two had been breast-fed up to the time of the onset of the illness. I am not maintaining that breast-fed infants do not develop otitis media, gastro-enteritis, and other infections, because we all know that they do, but to a much less extent. Thus Johnston, Brown, and Tisdall (1930) found that in only five cases of intestinal intoxication the children were breast-fed, while in 141 they were bottle fed. Dr. J. M. Smellie, in our own hospital, tells me that in only three out of 60 clinical cases of gastro-enteritis the infants were entirely breast-fed. Whether the breast-fed children develop these diseases or not, the point I want to make is that they practically always survive. It is my belief that the best insurance that a mother can adopt for her infant is breast-feeding, whenever it is possible, and particularly during those difficult first few months of life when infections are so dangerous.

My next point is so evident that I hesitate to mention it, but repetition sometimes emphasizes. The case that I have made against upper respiratory infections from which otitis media arises, has wide implications. Everyone admits that such infections are contracted from other persons. It cannot be too strongly emphasized that contact of an adult with an infant, while that adult is suffering from influenza, or the common cold, is exposing the infant to one of the gravest risks which it can encounter during its lifetime.

In an attempt to overcome any possibility of infections occurring in these infants while they are in the hospital for other conditions—being aware of the high mortality in the younger age-groups—we are shortly going to erect, in connexion with the Birmingham Children's Hospital, an Infant Department which will provide isolation for each child, and facilities for preventing any possible spread of infection by contact or carrier, and will have an adequate staff to ensure conditions of attention even better than those afforded in the best of homes.

It must be apparent from the conditions which I have reviewed that there is a great field for co-operation between the pediatrician and the ear-nose-and-throat surgeon. A more careful search of the upper respiratory tract of infants and children during examination by pediatricians seems to be indicated, and I think that earlier consultations and treatment by otologists, with careful management by physicians trained in diseases of children, is a possible means of obtaining better results in dealing with this disease.

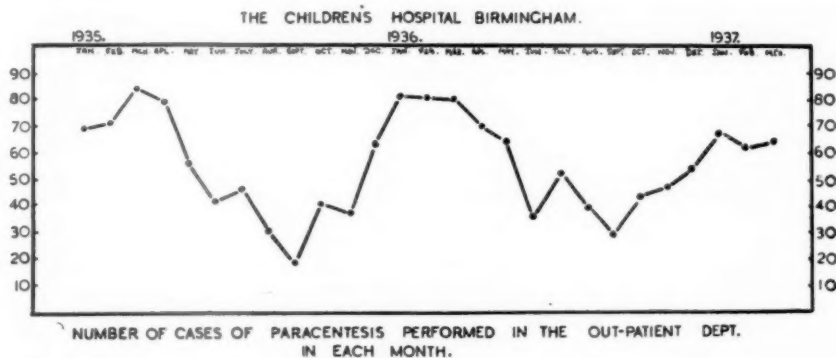
Otitis media, as found at post-mortem examinations in this series, has played a very large part as the aetiological, complicating, or final, cause of death in a great many of these children. There is not any doubt in my mind, after examining this large number of cases and finally analysing my results, that otitis media is a much more important condition in infancy and childhood than is commonly believed.

REFERENCES

- BROWN, ALAN, JOHNSTON, M. M., and TISDALL, F. F. (1930), *Can. M. A. J.*, **23**, 231.
CAMPBELL, E. H. (1934), *Arch. Otolaryng.*, **20**, 698.
CARMACK, J. W. (1930), *Ann. Otol., Rhin. and Laryng.*, **39**, 75.
CROOKS, J. (1936), *Arch. Dis. Childhood*, **11**, 281.
CULLOM, M. M. (1934), *J. A. M. A.*, **103**, 1695.
JEANS, P. C. (1926), *J. A. M. A.*, **87**, 220.
LIERLE, DEAN, M. (1927), *Ann. Otol., Rhin. and Laryng.*, **36**, 686.
MARRIOTT, MCK. (1928), *Arch. Otolaryng.*, **7**, 13.
TAGGART, W. B., and HARTMAN, J. I. (1930), *Ohio State M. J.*, **26**, 126.
WISHART, D. E. S. (1930) (in a paper by BROWN, A., et al.), *South. M. J.*, **23**, 107.

Mr. Stirk Adams: I wish to stress Dr. Ebbs' conclusion that the common cold is often the initial cause of a major disaster in infancy. The accompanying chart showing the number of children whose drumheads were paracentesed in each month, month by month, during the years 1935 and 1936 in the Casualty Department at the Children's Hospital, Birmingham, illustrates one aspect of this. These children were

not suffering from any exanthem other than the common cold, and although the figures include children up to the age of 12 years, approximately one-third were under the age of 2 years.



In the wide field open to us in this discussion I am confining myself to the problem of otitis in infancy, i.e. under the age of 2 years, when it complicates, or coexists with some other medical condition. I regard otitis and mastoiditis as identical in these children, and while a complete survey of the problem has not proved possible, owing to the difficulty of obtaining records, yet some indication of its extent has been obtained by an examination of the records of the 50 cases in which mastoid operations were performed on children under the age of 2 years, by my colleague, Douglas Marsh, and myself, in the Children's Hospital, in the years 1935 and 1936. They fall into two main groups. The first we can designate primary otitis, in that the only pre-existing illness was a common cold. This includes 35 cases, of which 29 were acute and six chronic. In three of these cases diarrhoea and vomiting occurred after operation, and because of the special importance of this symptom I have included these cases in a group in which the relation between diarrhoea and otitis will be discussed later in this paper. Most of these infants had a subperiosteal mastoid abscess on admission, and operation was followed by recovery without anxiety in all but two, who died. These were :—

I.—M. T., admitted, when 3 days old, September 11, 1936, with spina bifida. This was repaired surgically and healed.

One month later, while the infant was still in hospital, bilateral otitis media developed, and in spite of a double cortical mastoid operation on December 4, death resulted two months from its onset.

II.—B. F., aged 10 months. Admitted October 21, 1936. Developed a cold on October 18; on October 21 both ears were discharging. October 27: Cortical mastoid operations performed. The infant died on November 5.

Post-mortem examination revealed a thrombosis of the superior longitudinal sinus, and lobar pneumonia involving the right lower lobe. Pus was present in the maxillary antra, ethmoidal cells and both middle ears and mastoid antra.

There were also three patients operated on for recurrent otitis and one operated on for tuberculous otitis; all recovered.

In the group of secondary otitis, or otitis complicating some other illness, there were 13 patients.

TABLE I.

					Total	Result	
						Cured	Died
Primary otitis.	Acute	27	25	2
"	Chronic	6	6	0
Recurrent otitis	3	3	0
Tuberculous otitis	1	1	0
Secondary otitis							
To measles	4	4	0
" diarrhoea-and-vomiting	6	2	4
" bronchopneumonia	2	0	2
" meningococcal meningitis	1	1	0

I would draw particular attention to the diarrhoea-and-vomiting symptom complex in its association with otitis. To make the position clear we have to realize that the prognosis for infants developing diarrhoea-and-vomiting is that 30% will die. I am told that this is the proportion in my own hospital, and the figure shows little variation among other hospitals. Dr. Ebbs has pointed out that in all the children who had died from this condition and were examined post mortem there was evidence of otitis media. It has been suggested that this latter is a terminal infection, or else the effect of suction after death. I do not think we can accept either of these views, for the majority of these children have had a recognized otitis for weeks before death, and many of them have had a paracentesis performed, releasing exudate under tension. In its clinical course diarrhoea-and-vomiting in infancy is often acute in onset. Many patients respond rapidly to treatment, although a few children are lost in the first few days from the severity of the toxæmia. Some of these children, however, after an initial improvement, as a result of treatment by salines and blood transfusion, begin to go downhill, and at this stage otitis is recognized and paracentesis is performed. In spite of this and further transfusions the downward progress is not arrested, and a few days later the otologist is asked whether he thinks mastoid drainage should be performed. You will realize that by this time the physician is anxious that no focal infection should remain to prejudice the chances of recovery of his patient, yet the upset of a mastoid exploration may be more than the child is fit for. A difficult decision to make, as it is equally clear that the chances of improvement after a surgical drainage of the mastoid are not good, yet operation offers some hope for the patient. The following table gives the results obtained:—

TABLE II.

	Total	Cured	Died
Group 1: Acute otitis and D.-and-V. simultaneously	2	0	2
Group 2: Bronchopneumonia; otitis some weeks later; D.-and-V. late	2	0	2
Group 3: Primary D.-and-V. without otitis; otitis ten days later	4	2	2
Group 4: Primary otitis; intercurrent D.-and-V.	4	4	0

Groups 1, 2, and 3 were composed of cases in which the mastoid exploration was being carried out as a last resort, and in assessing the mortality of this group this fact should be borne in mind.

Group 1.—In the first group are two infants who developed acute otitis, and diarrhoea-and-vomiting simultaneously. In spite of all treatment they both died.

K. K., aged 8 months. Admitted August 19, 1935, for treatment for scurvy. He had been well until four months previously when he developed an illness which lasted three weeks and was diagnosed as meningismus. He recovered, but was never quite well and three weeks before admission had begun to cry with pain.

August 24 (five days after admission): Diarrhoea and a right ear discharge developed simultaneously.

August 24, 1935: Paracentesis.

September 9: Paracentesis.

September 12: Double cortical mastoid operation.

September 15: Patient died.

No treatment appeared to have any effect on the diarrhoea, although the scurvy had been cured biochemically.

B. B., aged 4 months. Admitted September 19, 1935. Had been under treatment at another hospital for the three previous weeks.

September 18: Otitis, and diarrhoea-and-vomiting appeared simultaneously. Double paracentesis.

September 22: Further paracentesis.

September 24: A bilateral mastoid operation.

The child survived until October 6, the diarrhoea persisting until the end.

Post-mortem findings.—Hæmorrhages present in the small intestine; three active ulcers also present in this region.

In classing these two cases as a group in which diarrhoea-and-vomiting and otitis developed simultaneously, the decision has been made on apparent clinical grounds. A further investigation, which has not yet been completed, suggests that in all cases in which diarrhoea and vomiting develop, a recognizable upper respiratory infection has been present prior to the development of the diarrhoea-and-vomiting syndrome.

Group 2.—In Group 2 there are two cases. In each otitis media developed some weeks after bronchopneumonia; diarrhoea-and-vomiting occurred as a late manifestation in the illness, and both children died.

D. R., aged 9 months. Admitted February 24, 1935. Had had bronchopneumonia February 1, 1935; recovered and was well.

February 24: Otitis media and meningismus. Double paracentesis.

March 9: Child dehydrated. Double paracentesis.

March 11: Double mastoid operation.

March 13: Child died thirty-two hours after operation.

Post-mortem.—Generalized pleurisy (right). Patchy bronchopneumonia (both lungs).

G. S., aged 11 months. Admitted April 4, 1935. Had been admitted to another hospital three weeks before, with bronchopneumonia.

March 15: Injection of left drumhead; right membrane thickened (but no paracentesis carried out until April 1, three days after high pyrexia).

March 28: Pyrexia. Onset of diarrhoea-and-vomiting.

April 1: Double paracentesis.

April 5: Bilateral mastoid operation: Child died twenty-four hours later.

Post-mortem findings.—Extensive bronchopneumonia. Infection of right maxillary antrum.

Group 3.—In the third group there are four cases, in each of which a primary diarrhoea-and-vomiting developed without otitis. In each otitis developed about ten days after the onset of diarrhoea-and-vomiting. Two of these children recovered and two died.

P. B., aged 5 months. Admitted August 5, 1935. History of diarrhoea-and-vomiting since August 1.

August 13: Paracentesis (right and left).

August 23: Right mastoid operation and bilateral antral proof puncture; both antra contained quantities of mucus. Child collapsed and died a few hours after operation.

Post-mortem findings.—Quantity of pus in maxillary antra; bronchopneumonia in both lower lobes. Pus in left middle ear.

H. S., aged 13 months. Admitted August 7, 1935.

History.—Off food for a fortnight before admission; vomited every day during this time.

August 10: Paracentesis (left).

August 11: Paracentesis (left).

August 12: Paracentesis (right and left).

September 2: Bilateral mastoid operation under gas-and-oxygen. Slow recovery.

September 26: Discharged from hospital.

J. P., aged 8½ months. Admitted December 16, 1934, with ileo-colic intussusception, which was successfully reduced at operation.

On December 29 it was noted that he had vomited occasionally for some days and had not taken all his feeds. Hunger stools had been present at first, afterwards, green watery stools. Ears normal.

January 8, 1935: Child dehydrated and right drumhead injected.

January 9: Diarrhoea-and-vomiting. Right paracentesis performed.

January 25: Profuse discharge from both ears.

February 1: Double cortical mastoid operation.

February 28: Discharged; well.

On January 5, 18, and 23, positive cultures of *B. dysenteriae* Sonne were recovered from the stools.

D. B., aged 5 months. Admitted September 17, 1936.

History.—Onset of diarrhoea September 10, 1936.

September 21: Right otitis diagnosed.

September 22: Paracentesis (right).

October 3: Paracentesis (right).

October 4: Right mastoid opened under novocain. Left paracentesis.

October 6: Child died, immediately after a 40-c.c. transfusion of blood intravenously.

Post-mortem findings.—Pus in left sphenoid, ethmoid and antrum, left middle ear and mastoid.

Group 4.—In the fourth group are four patients. Here the illness began with an otitis, and diarrhoea-and-vomiting occurred later. All recovered.

C. P., aged 1 year and 9 months. Admitted May 22, 1935. A fortnight before admission a nasal discharge had developed.

May 18: Spontaneous discharge from left ear.

May 19: Paracentesis (left).

May 22: Tender left mastoid. Operation: Left cortical mastoid and right paracentesis.

July 11 to July 21: Enteritis.

August 3: Recovered.

F. S., aged 6 months. Admitted November 23, 1935. History of ear-rubbing (right) for ten days previously and now swelling right mastoid.

November 23: Right cortical mastoid and right paracentesis.

November 30: Diarrhoea.

December 6 to December 12: Diarrhoea.

December 29 to January 10: Diarrhoea.

January 25: Discharged, cured.

B. G., aged 8½ months. Admitted April 2, 1936. History of bronchitis a month before and otorrhoea for three weeks before admission. Swelling behind right ear two days.

April 2: Right cortical mastoid.

April 7: Diarrhoea.

April 18: Left paracentesis.

May 7: Readmitted. Further discharge from left ear and right mastoid, and persistent diarrhoea-and-vomiting.

May 26: Finally discharged.

M. H., aged 9 months. Admitted May 19, 1935. Measles had occurred three weeks before and the right ear had discharged for a fortnight. Vomiting occurred during the week before admission but no diarrhoea.

May 21: Cortical mastoid right ear.

June 6: Diarrhoea.

June 14: Cortical mastoid left ear.

June 27: A note was made that, in spite of repeated blood and saline transfusions, the child was still very pale and dehydrated.

July 1: Diphtheria recognized in nasal swab.

July 5: Child better.

July 31: Child discharged, recovered.

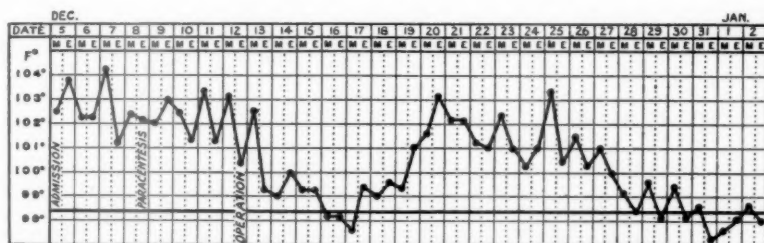
That a history of measles as a cause of otitis does not justify a serious prognosis is proved by three other cases in which a cortical mastoid operation had been performed for otitis supervening on measles, and in which the patients recovered without the development of diarrhoea-and-vomiting.

From so small a series as this the conclusions drawn must be tentative. In spite of the fact that in Groups 1, 2, and 3 out of eight patients operated on, six died, I still think we are justified in carrying out operation when the patient is failing to respond to medical treatment and otitis is known to be present, especially when there are symptoms of aural irritation, e.g. ear-rubbing, and head-rolling. Before the operation is carried out the child must be brought to the best possible condition by blood-transfusion or subcutaneous salines, as thought necessary. My preference is for operation under local anesthesia, using a small quantity of 1% novocain. During the operation the child shows no distress and usually sucks vigorously at a bottle containing sterile glucose and water. In the fourth group, in which diarrhoea-and-vomiting occur as a late manifestation, treatment is usually successful in arresting it. There is, however, another group not represented in this series, in which a patient has been admitted to hospital with otitis for which paracentesis has been performed. Sometimes diarrhoea-and-vomiting will occur, while both ears are discharging profusely, and this I regard as an indication for opening one or both mastoids as soon as possible.

In general, an acute otitis media may complicate any medical condition of infancy. It is always important, and treatment of the otitis may be the determining factor in the recovery of the child. As an illustration of this I quote a last case in which a child suffering from meningococcal meningitis—which had been fully controlled by medical treatment—developed a bilateral otitis media which prejudiced his recovery. A double cortical mastoid operation changed the picture entirely and full recovery ensued.

G. B., aged 18 months. Admitted on December 5, 1935, with meningococcal meningitis of four days' standing. Between December 5 and 9 many lumbar punctures were carried out and large doses of anti-meningococcal serum were given.

December 9: Cerebrospinal fluid had become clear, but the persistence of the temperature



G. B. Temperature chart.

suggested the aural infection which was diagnosed on inspection. A bilateral paracentesis was followed by a profuse discharge but in spite of this the pyrexia still persisted.

December 12: Both mastoids were opened, and following this the temperature became normal.

December 17 to December 31: Suffered from the effects of a generalized serum rash, the ears at this time being perfectly satisfactory.

Dr. C. E. Scott and Dr. R. B. Lumsden: This paper is based on a consideration of 564 cases of suppurative otitis media occurring in children under 5 years of age, in the Ear and Throat Department of the Royal Hospital for Sick Children, Edinburgh, during the years 1934 to 1936, inclusive. Of these, 145 occurred in children under 1 year of age and 419 in children over 1 year but under 5 years. We will briefly mention several points which have particularly impressed us in our work with children, and which have been brought out in the analysis of our cases.

Table I shows the number of cases, &c.

TABLE I.—ROYAL EDINBURGH HOSPITAL FOR SICK CHILDREN.

Cases of Suppurative Otitis Media in Children under 5 years of age, 1934 to 1936 inclusive.							
Under 1 year	1 to 5 years	Male	Female	Right	Left	Bilateral	Total
145	419	288	276	185	179	200	564

A cause of onset other than acute coryza was assigned and recorded in 46 cases:—

Under 1 year:	Measles	1	
	Tonsillitis	1	
1 to 5 years:	Tonsillitis	7	
	Removal of tonsils and adenoids	4	
	Removal of adenoids	2	
	Acute bronchitis	1	
	Pneumonia	2	
	Intranasal antrum operation	2	
	Measles	17	
	Scarlatina	8	(1 "contact")
	Whooping-cough	1	
						46	

Etiology.—Acute coryza was found to be the most common cause and we only record 46 cases in which a definite cause other than coryza could be stated. At the same time, we have been impressed by the frequent inability of a parent to ascribe any definite cause.

OPERATION CASES.

Under 1 year	34 cases
1 to 5 years	120 "
Total						154

NUMBER OF OPERATIONS PERFORMED.

		Myringotomy	Schwartz	Modified
Under 1 year	...	10	29	...
1 to 5 years	...	28	107	3
Total		38	136	3

Myringotomy followed by Schwartz mastoid operation (included in table above).

Under 1 year	2
1 to 5 years	12
					14

Operation cases.—Of our total of 564 cases, 154 required operation, 34 being under 1 year of age and 130 over 1 year but under 5 years. Considering the two age-groups together, of 38 myringotomies performed, 25 ears were dry at the last examination; 13 failed to report after leaving hospital. 136 Schwartz operations were carried out; 132 recovered, four died, of which three were under 1 year, and one over 1 year. Fourteen of these were preceded by myringotomy. A dry ear and a well-healed wound resulted after 66 of these operations; in 21 the ears were still discharging when last examined, and 28 cases were lost sight of (country patients).

TABLE III.—DURATION OF OTITIS MEDIA AT TIME OF SCHWARTZE OPERATION.

16 cases under 1 year :	Shortest	2 days
	Longest	300 "
	Average duration	46 "
74 cases from 1 to 5 years :	Shortest	2 days
	Longest	540 "
	Average duration	37 days

BACTERIOLOGY.

Schwartz Operations—

Under 1 year (13):	<i>Streptococcus hæmolyticus</i>	7
	<i>Str. viridans</i>	1
	<i>Pneumococcus</i> (type not known)	4
	<i>B. influenza</i>	1
1 to 5 years (29):	<i>Str. hæmolyticus</i>	26
	<i>Pneumococcus</i> (type not known)	2
	<i>B. influenza</i>	1

This table shows the duration of otitis media at the time of the Schwartz operation, also the bacteriology in a proportion of cases.

Complications.—Two developed erysipelas; four developed measles; four developed scarlatina; of these four one, aged over 1 year, had also an associated retropharyngeal abscess. Two developed kidney trouble.

In one case (under 1 year) a facial paralysis was present at the time of operation, the auricular glands were enlarged, and the child had been bottle-fed. Clinically this case closely resembled a tuberculous infection, but no bacteriological or histological evidence was found to support this diagnosis. A radical operation was subsequently necessary.

Another case under 1 year presented interesting features, which we think merit attention. This child was admitted to hospital with marked œdema and tenderness over the mastoid process. The temperature was over 100° F. and a definite bronchitis was present. The tympanic membrane, however, was practically normal in appearance and there was no suggestion of sagging of the posterior meatal wall. At operation, definite infection of the mastoid cells was found, and a swab of pus taken gave a pure culture of *Streptococcus hæmolyticus*. The child died, and at the post-mortem examination the blood sinuses were found to be healthy but there were multiple pyæmic abscesses in the lungs and abdominal organs. We suggest that this case is one of blood-borne mastoid infection.

TABLE IV.—INTRACRANIAL COMPLICATIONS. LATERAL SINUS THROMBOSIS.

	Cases	Recovered	Died
Under 1 year ...	2	—	2
1 to 5 years ...	2	1	1
	4	1	3

Intracranial complications.—In respect of these, we appear to have been somewhat fortunate during the period under consideration, thrombosis of the lateral sinus being the only one encountered in these age-periods.

In considering the value of myringotomy, as revealed by our figures, 52 myringotomies were performed. Of these cases, 14 required a subsequent Schwartz operation. Of the total number of cases, we find that 22% had a Schwartz operation performed without any previous myringotomy; 21% of cases in which myringotomy was performed required a subsequent Schwartz operation. This 1% difference suggests that myringotomy is not an important factor in the avoidance of subsequent mastoid operation in these age-groups. We do not, however, interpret this as an argument against the value of myringotomy, as another factor must be considered, namely the period required for ultimate resolution and recovery of hearing.

The value of myringotomy when performed on the intact drumhead in a case of acute otitis media is well established. When performed in the presence of a small

perforation, when drainage was considered to be inadequate, we have been disappointed in its efficacy. In connexion with this operation, we have been impressed with the deceptive appearances of the infant drumhead in acute otitis. It is so often not the textbook inflamed, bulging drumhead, with perhaps the yellowish tinge indicative of imminent perforation. Rather do we find it lustreless and opaque, with little or no apparent bulging; such cases are frequently seen in medical wards in which no other cause can be found to account for a continued pyrexia. Myringotomy generally reveals pus, and resolution of temperature follows. With regard to the Schwartze operation cases: Many of the operations were performed in the absence of acute mastoid symptoms but discharge was persistently profuse; the temperature generally settled, but the pulse-rate remained raised.

In just such cases we have not the guidance which is to be derived from hearing tests, which are of such value in older patients. It is all the more important, therefore, that we should keep the preservation of this function constantly before us.

In a small series of cases we have been impressed by the value of skiagrams of the mastoid, even in children under the age of 1 year, when considered as part of the whole clinical picture. Clouding of the mastoid cells is generally found in all cases of early acute otitis media, but it is later, when definite breaking-down of the cells may be shown, that they prove of assistance.

The value of tonsil and adenoid removal has not been overlooked in our treatment, but we feel that this subject alone would provide material for a discussion.

TABLE V.—TUBERCULOUS OTITIS MEDIA.
(9 cases.)

Under 1 year 7	1 to 5 years 2	Male 5	Female 4	Right 1	Left 4	Bilateral 4	Total 9
<i>Results</i>							
Under 1 year: Alive (all discharging)	5	Dead	...	2
1 to 5 years: Alive	0	Dead	...	2

All proved histologically or bacteriologically.

Definite history of bottle-feeding in 4.

No record in 5.

Facial paralysis in 3—all under 1 year.

We cannot conclude without referring to a particular type of otitis met with in the age-groups under discussion, namely tuberculous infection of the middle ear. This condition was at one time fairly common, but is now apparently on the decline. During the years under consideration, we have only been able to collect a series of nine cases and as time is limited, we will only refer to a table giving some particulars of this series.

The President showed a series of slides, including an otoscopic picture of what Dr. Le Mée called "unsuspected" otitis. The child had been in a medical ward for a fortnight, and had had all his "systems" examined, except the ear; all with negative results. Then the otologist was called in; paracentesis was performed, and improvement at once followed. He also showed a chart, prepared more than ten years ago, to show the extraordinary prevalence of otitis; the frequency in infants dying from all causes varied from 75% to 96%.

Another chart exhibited showed the age-incidence of otitis media, and he, the President, would point out it strikingly resembled one of the charts shown, earlier in the discussion, by Dr. Ebbs. There was a rise just before school age; apparently when the child went to school it came under examination by the school medical officers, and otitis was more likely to be discovered.

Why was otitis so common in infants? One reason was that when the child was born there remained, in very many cases, fragments of embryonic connective tissue, such as that which filled the ear during embryonic life, and which usually became

absorbed at or at about the time of birth. Portions of this tissue might remain in the corners of the tympanum, and embryonic tissue was very liable to become infected. A slide shown indicated clearly the malleus and part of the incus embedded in such embryonic tissue.

He had been relieved to hear Dr. Le Mée and Dr. Ebbs say that on incising a suspected tympanic membrane, pus was not always found, because hitherto he had blamed himself when no pus appeared on incision, and when it appeared afterwards it had been considered to be due to infection by the surgeon!

He asked under what conditions Dr. Mée found what he called the "frosted" tympanic membrane, dotted with little white grains. He, the speaker had seen this appearance in older children, and regarded it as a milder type of infection.

Dr. Le Mée had said that he performed the mastoid operation on infants in two stages and he (the President) would like to know why. He knew that in France there was a fear of the mastoid operation for the very young, and he would like to know whether it was a fear of the anaesthetic, or of the actual operation.

Dr. Ritchie Rodger had said that in the cases of pulmonary infection, speed in operating was essential; did he consider that a mere incision would suffice, followed, if necessary, by the bone operation at a later date? A number of practitioners held that in infants mere incision of the abscess was sufficient to cure mastoiditis.

He agreed with Dr. Ebbs that the mastoid operation was seldom justifiable in cases of gastro-enteritis; he had operated in a number of these, and was not satisfied that the results were better than if the cases had been left alone. A good deal of work remained to be done in order to determine the relationship of otitis to malnutrition, gastro-enteritis, and pulmonary infection.

One of the earliest otoscopic signs of otitis in infants was the disappearance of the cone of light.

He did not think that the X-ray picture was of much value in mastoiditis in children; any value it possessed was only anatomical, showing the position of the lateral sinus and the degree of pneumatization. It was of no value at all unless both sides were radiographed and compared.

Mr. E. Watson-Williams said that he had devoted special attention to otitis media in the very young ever since 1929 [1] when he had analysed a series of cases. He then found that the first year of life provided more cases needing mastoid operation for acute infection than any subsequent year, and that the first two years supplied the great majority of first attacks of otitis media [2] [3].

He had been particularly interested in three of the points Dr. Le Mée had made. First that otitis media meant infection of the whole middle-ear tract including the mastoid antrum and cells [2]; there was no barrier between these and the tympanum and they became infected within a few minutes of infection of the latter. Secondly, his indication for myringotomy—one sleepless night [4]. Thirdly, that the mastoid operation on babies should be short; his (the speaker's) own plan was "a minute a month", i.e. for a seven-months'-old baby, the operation must be completed in seven minutes from incision to stitches. A twenty-minute operation was a severe test for a young baby.

REFERENCES

- 1 WATSON-WILLIAMS, E., *Practitioner*, 1929, 122, 36.
- 2 Id., *Brit. M. J.*, 1933 (ii), 329.
- 3 Id., in "Modern Treatment in General Practice", London, 1934, p. 194.
- 4 Id., in Hamilton Bailey's "Emergency Surgery" (1st ed.), Bristol, 1931, Vol. 2, p. 103.

Dr. McNair Scott said it seemed to him that routine examination of the ear in infants with upper respiratory infections often revealed a red and swollen drum. A certain number of these children had obvious symptoms from the ear, such as pain and restlessness, and in these, myringotomy was obviously indicated; in others an

ear with similar appearance gave rise to no symptoms, and would often quiet down without any treatment. In infants with diarrhoea-and-vomiting, again, one found in some an obviously bulging drum behind which was pus; in others the drum was reddened, and no pus was released on incision. In the children with diarrhoea-and-vomiting one felt compelled to incise a drum which, in the absence of these symptoms, one would have been inclined to leave alone.

He would like to ask his surgical colleagues (1) whether any harm ever came of incising a drum unnecessarily, and (2) whether they felt that, otologically speaking, there was anything specific about the otitis in infants with diarrhoea-and-vomiting which suggested that a different form of therapy from that in otitis without this complication should be employed.

In children with pneumonia it was very common to find that the ear-drum was red and often it might be swollen. In the majority of such cases the ear trouble subsided after the crisis without therapy. However, he had the impression that Type III pneumococcus was particularly liable to cause trouble in the middle ear, and that ears affected with that organism usually had to be opened. He wondered if Dr. Ebbs, in his study of otitis media, had typed out the pneumococcus obtained, and what his results had been.

Dr. Le Mée (in reply) said that he performed the mastoid operation in two stages in these very young patients because he and his colleagues had seen, a few years ago, many cases in which, a few hours after the operation, the patients had high fever and were very pale, so that complication was feared. His colleagues had also published reports of cases in which a high temperature had developed after the mastoid operation, but since the operation had been carried out in two stages such a complication had not been encountered. When first the mastoid was opened limitation of the purulent process occurred, and when the bone was opened it was found to be soft. It was not the general anaesthesia which was feared because, in these very young patients, anaesthesia was produced by applying cold water or ice to the back of the ear for five minutes; opening the bone was then not painful. Shock was a very important matter in the case of infants, and should be avoided as much as possible.

Dr. Ritchie Rodger (in reply) said that when he had spoken of speeding the operation, he had not been referring to the simple incision; he had really meant that no time should be wasted by the operator. Sometimes the complete operation was carried out in twenty-five minutes.

Section of Urology

President—BERNARD WARD, F.R.C.S.

[April 23, 1937]

Imperfect Migration of the Testicle: The Surgical Problem

By G. GREY TURNER, M.S.

THE renewed interest in this subject is very refreshing, for only a few years ago the great majority of surgeons were content to accept the position that operative treatment was usually unsatisfactory. In quite recent editions of some of our well-known textbooks stress is laid on the disappointing results of operation, and when the condition is unilateral castration is advised. I must myself admit that I had almost accepted this position until I read the article "On the Pathology and Treatment of the Retained Testis in Childhood", by A. H. Southam and E. R. A. Cooper,¹ I was so much impressed by the statements made by the authors that I set out with renewed enthusiasm, and the success which has attended my efforts since then has been encouraging. The following table reflects the influence of their teaching in my own practice:—

THE TREATMENT OF A SERIES OF CASES DURING TWO PERIODS

		Orchidopexy		Castration
1920-1927 i.e. 8 years	...	None	...	17
1929-1932 i.e. 4 years	...	24	...	4

During the years in question I made no special effort to secure this type of anomaly for treatment so that the numbers are few, but that in no way detracts from the deduction which is to be inferred.

Although we are all so interested in this condition, everyone must feel the hampering influence of the lack of knowledge as to its cause. The problem is an age-old one, but we still have to admit that it is as yet unsolved. There are two views that hold the field—that expressed by John Hunter in "The Animal Economy" published in 1786, where he wrote "It is not easy to ascertain the cause of this failure in the descent of the testicle; but I am inclined to suspect that the fault originates in the testicles themselves". The other was expressed by Owen H. Wangenstein, when he wrote in 1927 (*Archives of Surgery*, Vol. 14) "The undescended testicle owes its imperfection to its position". The not infrequent favourable effect of hormone

¹ *Lancet*, 1927 (i), 805.

therapy, which appears to act by causing increased growth and activity of the genitalia, lends some support to the original view of John Hunter, and this is also borne out by the cases in which we know that the late descent of the testicle can be verified. On the other hand, every surgeon who is acquainted with his after-results must be aware that, even after a successful anatomical re-position, in a good many cases (*see fig. 1*) the organ fails to develop in the way that might have been expected if the only stimulus required was the normal nevironment to be found in the scrotum, as suggested by Wangenstein. As the result of much experimental research this surgeon suggests that it is the lower temperature and the variations of temperature to which the organ is subjected in the scrotum that account for its full development there. He makes reference to many observations and experiments on



FIG. 1.—Lack of development of testicle after satisfactory scrotal reposition at 13 years of age. Photograph taken at 21. Testicle small and soft, and with only modified sensation.

lower forms of animal life. But surely there are other factors than simply this question of temperature. Probably the testicle, freely dependent in the scrotum, is subject to slight vascular congestion, and it must be affected by the movements of the body and by the gentle caressing action of the contracting dartos muscle. These are factors well known to stimulate testicular activity and might be expected to aid development. Again, we do know, from a considerable experience of the Keetley operation, that when the organ is buried in the thigh it frequently develops, and there again some of the above-mentioned factors may be involved as well as a more uniform and probably increased temperature. There must also be the stimulus supplied by the movement of the body when walking, which will presumably act like oft-repeated manipulation or massage (*fig. 2*).

Much has been said about the late descent of the testicles, that is, some years after birth. I have always taken a keen interest in this matter but have never been satisfied that descent occurs later than the age of three years, and I have always thought that, if it is going to take place, it can only be expected well within this period. But this is a matter in which, perhaps, detailed information from school medical officers, who have the opportunity of examining large numbers of young boys, may justify some other conclusion.

In the treatment of imperfect migration of the testicle, we are probably dealing with a group of cases in some of which the question of hormonal influence on general development is very deeply concerned, and I am inclined to think that the unilateral cases and the bilateral cases may really be in entirely different groups. In the unilateral, the scrotum is always developed, but the testicle which is descended, and the penis, may be small or abnormally large but very rarely grossly undeveloped.



FIG. 2.—Patient after first stage of the C. B. Keetley operation.

In the bilateral cases, there are certainly two groups; in one the external genitalia are very small and ill-developed, with scarcely the appearance of a scrotum, while in the other the penis is fully, or sometimes abnormally, developed and the scrotum is normal except for the want of its tenants. It is the patients in the latter group who have been said to beget children. In both groups secondary sexual characteristics are present, though not equally developed. It is unlikely that the underlying problem is the same in both, for in the one there is obviously some general lack of development of the whole genital apparatus, whereas in the other this lack appears only to affect the testicle. In the former some general endocrine stimulus would appear to be the most important requirement, while in the latter the mechanical assistance of operative surgery may supplement or even supplant such treatment.

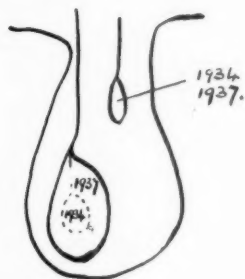


FIG. 3.—Left undescended testicle. Operation at 12 years of age. A year later, both testicles in good position but very small. Three years later the unaffected testicle developing normally while on operated side development was arrested.



FIG. 4.—A H., now aged 31 and the father of three children. Double orchidopexy sixteen years previously.

It has been customary to assume that if a testicle, however small, can be successfully returned into the scrotum, it will develop normally in response to awakening function. This unfortunately does not represent the whole truth for I have often been disappointed in the subsequent progress of cases in which I have been satisfied that the testicle has been satisfactorily transferred by surgical measures to its proper place (fig. 3). The same sort of assumption has been made with regard to cleft palate, though it is an undoubted fact that an excellent anatomical restoration after operation, even when completed before the child has learned to speak, is not necessarily followed by a perfect functional result. In dealing with the testicle I have found that if after re-position the organ is going to develop, it does so almost at once, and if it does not do so then probably development will not occur as a delayed feature. Only time and very careful observation will show whether or not development is more likely to occur when the organ is buried in the thigh than when it is simply placed in its normal scrotal bed. In a good many cases in which the replacement of the organ in the scrotum has been particularly successful, it is probable that the surgeon has been dealing with an ectopic testicle, rather than one which has failed to descend. In many cases the inguinal testicle is very well developed, with regard not only to size and consistence, but also to anatomical form. In those cases in which the testicle has come through the external ring, it often turns upwards and outwards and lies on the external oblique above the ring. If in these cases it is accompanied by a hernial sac, it represents one of the varieties of interstitial hernia. This particular type of case is most amenable to surgical intervention, and some of the best results have followed when this has been the condition found (fig. 4). I am doubtful if hernia is so frequently associated with undescended testicle as has usually been supposed. There can be no question that there is constantly a process of peritoneum surrounding the testicle, which is exceedingly like a hernial sac, but I have very often been quite unable, even after punctilious care, to demonstrate any actual communication with the peritoneal cavity. This is a matter of some small practical importance, because we have often assumed that the presence of a soft swelling in association with the testicle has meant that there is also a hernia, and this supposition has prompted surgical interference at an age which is probably not the best for the attempted re-position of the testicle.

The symptoms sometimes attributed to the undescended testicle are often considerably exaggerated. In the majority of cases there are no symptoms, and I should say that as a rule it is an awakening sense of parental responsibility which has dictated the search for advice, rather than any symptoms to which the condition has really given rise. The imperfectly descended testicle is more liable to torsion than the normally placed organ, but it is certainly no more exposed to injury or inflammatory trouble.

Although the treatment by hormones has been followed by a very encouraging measure of success, there are many cases in which such treatment fails, and there are others in which operation holds out so good a prospect that it may well be the first choice. The latter cases are in boys who have arrived at puberty, or young adults in whom one testicle has already descended and is well developed, and in whom the retained testicle can be felt lying in the inguinal canal and is of reasonable size. If hormones fail after a twelve-months' trial, then operation should be undertaken. We want to know if treatment by hormones will make a testicle develop after it has been brought into the scrotum by surgery but seems reluctant to mature. We also want to know if a testicle has a better chance to develop when placed in a pocket in the thigh, after the method of Keetley, than when merely temporarily attached to the thigh by a temporary fixation suture.

The age of election for the active treatment of imperfect migration has been a moot question, and I am inclined to think that in the past I have interfered surgically at too early an age. Those who are most competent to lay down a dictum

seem to think that nine years is the proper age at which to begin the treatment by hormones. If that is so, then a year may well be allowed to elapse so that this treatment may have a proper trial. If at the end of that time the testicle has not come down I would be prepared to operate in the case of well-developed and actively growing boys, but if these conditions are not present, I think the operation would have a better chance of success if deferred even till as late as 14 years of age. At this latter time the testicle, in any event, ought to be ripe for development, and will presumably be better able to overcome any difficulties that may be imposed upon it by the necessary slight trauma of operative interference. But there is the question of the patients who do not present themselves until after puberty, and for them I have never refused to consider operation, whatever the indication. In bilateral cases the prognosis depends upon the genital development as shown by the condition of the penis and scrotum and possibly the sexual sensations. If the testicles are inguinal, they are often of reasonable size and can be brought into the scrotum without tension. If, on the other hand, they have not reached the inguinal canal, it is often impossible to mobilize and elongate the cord so far as to get them down. For psychological reasons it is well worth while making a great effort, certainly on one side. Either testicle, which cannot be got down to the bottom of the scrotum, should be replaced in the peritoneal cavity or the extraperitoneal tissue and we should not allow the possibility of malignant development to determine or control our management of these cases. It is impossible to deny the probable truth of surgical tradition or the sterner facts of statistical research, but at the same time I must confess that only twice in a surgical lifetime have I seen the development of malignant disease in association with an undescended testicle.

The unilateral cases present an easier problem, for it is usually possible to get the organ satisfactorily down. If the difficulty is insuperable and the opposite testicle is fully descended and normally developed, then the imperfect testicle may be removed with some confidence that the general economy of the patient will suffer no detriment.

Should a hernia in association with an undescended testicle be operated upon when discovered, or should the interference for the hernia be deferred until the optimum age for the treatment of the testicle? It may be that the development and growth of the hernia may even aid the elongation of the cord and assist the subsequent operation for re-position. If this is not true, then probably it would be better merely to operate on the hernia by the removal of the sac at whatever age such interference was considered to be wise, while the operation on the testicle is deferred until the optimum age, some time between 10 and 14. In carrying out the actual operation for re-position of the testicle there is, of course, an advantage in having the hernial sac, which is a useful handle when we come to separate the elements of the cord from the peritoneum. But there again the operation has to be done often enough when there is no sac.

Although some surgeons speak of operating for imperfect descent in stages, I have found that this plan adds to the difficulty rather than otherwise and am sure it is better to defer the operation on the testicle until the time of election rather than make a premature attempt.

To summarize: I would suggest that probably the optimum time for an operation is between the ages of 10 and 14, but that if the patient does not present himself until after that age, the operation is still worth while. Even in adults, if the organ is well developed it may be replaced in the normal position with some psychological advantage, or perhaps to fulfil the requirements of one of the public services.

So far as the actual technique of the operation is concerned, the essential point is the thorough mobilization of the cord and especially the vas. To enable this to be carried out properly, the inguinal region must be freely exposed and the external oblique divided to well above the position of the internal abdominal ring. The parts must first be identified and any hernial sac exposed, isolated, and freed from the

cord, but it should be retained as a handle during the process of mobilization and only ligatured off when this stage is complete. The vas (as can be seen from an inspection of the inner aspect of the pelvis in the cadaver) takes what appears to be an unnecessarily long course to reach the inguinal canal, and for some reason it is closely attached to the peritoneum. This course can be shortened by freeing it thoroughly from the peritoneum right into the depths of the pelvis and making gentle traction upon it after it has been thus freed. The vessels of the cord are usually longer, but their course can be shortened in the same way, using very gentle traction and most careful separation from the cellular tissue, aided perhaps by gauze stripping and only using scissors under the guidance of the eye. But the mobilization must be very thorough and painstaking, and usually carried far beyond the confines of the inguinal canal, and great care must be taken not to damage the vascular supply during this process. Division of the spermatic artery is always followed by atrophy of the testicle, and is a step which ought never to be taken if the organ is to be preserved. I have never divided the deep epigastric artery, but have sometimes shortened the route to the scrotum by making a track behind the artery which the testicle and cord can be made to traverse. This can readily be done and I do not think that there need be any hesitation in adopting the plan if the interests of the patient justify the step. After the cord is sufficiently mobilized and elongated, the next step is to open up the corresponding half of the scrotum by blunt dissection with the finger. If the testicle can then be placed in the scrotum without the least tension on the cord, it is sufficient to fix it temporarily to the thigh on the same or the opposite side. The fixation stitch is of silkworm gut and is passed through the testicle, the scrotum, and the skin of the thigh. It will have served its purpose in a fortnight and can then be removed. Should there be tension on the cord after the fullest possible mobilization, then the testicle is best fixed in a pocket in the thigh, after the method of C. B. Keetley (fig. 5, p. 84). This plan is also spoken of as Torek's method. As has already been mentioned, it probably has advantages other than the secure fixation which it assures. The question of how long the organ should be allowed to stay in the thigh is not one that can be easily settled, but I have seen no evidence that the testicle suffers because of residence in its temporary lodging and I should say that from three to six months was the most suitable period. In some cases even an abdominal testicle may be brought down, after adequate mobilization under the guidance of the eye, and if this is exceptionally difficult, it may be accomplished by the extraperitoneal route devised by Mr. A. K. Henry for certain cases of hernia.

The investigation of these cases is worthy of more care and attention than they often receive, for it is very easy to be deceived about the position of the testicle in young boys, especially when the cremaster is unusually active. In these circumstances this muscle may draw the testicle right up into the inguinal canal and may simulate the condition of inguinal retention. At other times in the same patient, the testicle may be found lying in its normal position in the scrotum. This condition is sometimes spoken of as the "retractile testicle", but the circumstances often justify the appellation "elusive testicle", which I prefer to use. When treatment by pregnyl or other hormone preparation is so freely advised and is supported by the alluring advertisements of drug houses, it is most important to utter this warning. I have no doubt that many examples of the elusive testicle are being treated by hormones as though they were cases of imperfect migration and, of course, with striking success! Surely it is unnecessary to say that the merely elusive testicle requires no treatment whatever.

In order that the problems associated with this fascinating subject should be properly worked out, it is essential that the cases should be most carefully examined and recorded in detail. If we are to accumulate accurate information, nothing less than the particulars set out in the following scheme will suffice.



FIG. 5.—Boy of 13. Testicle at external ring but very small. Orchidopexy with fixation to thigh. Separation three months later. Testicle developing satisfactorily. (Operation by G. Y. Feggetter.)



FIG. 6.—Perineal testicle. Man of 48, the father of eight children. Except that he was unable to ride a bicycle, had no disability.

INVESTIGATION OF CASES OF IMPERFECT MIGRATION OF THE TESTICLE.

*What we want to know.**Before operation.*

- History. Family history.
- Symptoms.
- General appearance, development, weight, temperament, &c.
- Local position, size, shape and condition of testes—both sides. Presence of hernia or hydrocele.
- Condition of scrotum and penis.
- Sexual condition.*

At operation.

- Exact position, condition, size and consistence of testicle (? piece for section).
- Presence of hernial sac or hydrocele.
- What is done in exact detail.

After operation.

- Position of testicle, size, mobility, consistence, sensation.
- General development and function of sexual organs.
- Emissions; spermatozoa; virility—potency—parenthood.
- Any hernia.
- General condition.

* When the patient is of the age to justify the inquiry.

This seems an opportunity to place on record a very unusual example of ectopic testicle (fig. 6). The patient came to hospital to seek advice concerning a right inguinal hernia. He made no complaint about the abnormally placed testicle, which was only discovered on routine examination. Operation was advised for the hernia, but the man did not wish the perineal testicle to be interfered with.

Dr. R. E. SMITH, speaking as a school medical officer, said that he had under observation some 600 boys between the ages of 13 and 18 in one school, and some 400 boys between the ages of 9 and 18 in another; and the number of boys with undescended testicles in the former school was very much less than that in the latter. In six years he had collected 23 cases, which he classified thus:—

UNDSCENDED TESTICLES.		UNDSCENDED TESTICLES WHICH HAVE SINCE DESCENDED.	
Age at present		Age at which patient first came under observation	Age at which testicle descended
9			
11			
11½			
12	Has recently had operation, bringing testicle into scrotum.	8	13½
12		12	12½
13		12	13½
13	Descending.	12	14
14	Puberty starting.	13½	14½
14	Puberty starting.	13½	13½
14	Has had operation for right inguinal hernia.	13½	14½*
14	Descending with pregnyl.	13½	16½†

* This boy had also late descent of the canine teeth.

† This boy has a general endocrine dysfunction.

FAILURES

Boy aged 16: Operation in 1932. Atrophied testis removed.

Boy aged 15: Operation when aged 8 for undescended testicle; unsuccessful.

Several courses of pregnyl unsuccessful.

Boy aged 17: Testis has enlarged under treatment with pregnyl but will not descend.

Operation on May 1. The testicle had ridden over the internal inguinal ring. With difficulty it was brought down into the scrotum and anchored there through the septum.

Those testicles which came down into the scrotum naturally appeared to be normal in every way with one exception, that of a boy who, while at camp, reached out for something, felt a sharp pain in the groin, and then noticed his testicle had descended. This testicle was considerably smaller than its fellow.

He had come to the conclusion that biological changes occurring at puberty caused the majority of these imperfectly descended testicles to come down into the scrotum. The same hormone was probably responsible for the mastitis of puberty, which was a fairly common phenomenon. He felt convinced that the right line of approach was to leave such testes to nature until puberty, provided ectopic testes could be excluded. If no change occurred at puberty, then oestrin should be given in full doses. If this was unsuccessful, a surgeon's aid should be obtained to discover whether there was some abnormality preventing the testicle's descent.

Section of Dermatology

President—H. W. BARBER, M.B., F.R.C.P.

[May 20, 1937, continued]

Benign Lymphogranuloma.—S. M. WHITTERIDGE, L.R.C.P., M.R.C.S.
(introduced by the PRESIDENT).

E. A. female, aged 36.

Family history.—Father died at age of 65, of tuberculous meningitis. A sister had psoriasis.

Previous diseases.—Only one of note—psoriasis since childhood.

Present disease.—In 1929 a small nodule, about the size of one of the old threepenny-bits, appeared on the left cheek. A diagnosis of lupus vulgaris was made, and the lesion cleared up under Finsen lamp treatment. At this time facial paralysis suddenly developed; this, over a period of four years, gradually disappeared. In 1936 there was a recurrence of the facial symptoms, associated with giddiness and vomiting. In addition there was weakness of the left leg and no control over walking. Six months after the first skin lesion had cleared up—that is in 1930—a red patch developed on the right side of the nose. This was treated with the Finsen lamp but did not improve. In 1934 the patient began to notice coldness of both hands, which were red and so painful and swollen that she was unable to bend them. The nails became thin and friable.

On admission.—There was a deeply indurated red patch over the "butterfly" area of nose and cheeks, with many dilated venules and adherent scales. The nose was enlarged and deformed, and there were many small brown vesicles. There were also patches over both eyebrows, and other areas on the wrists, ankles, and abdomen.

The ends of all the fingers had glossy atrophied skin and a number of small ulcers. The nails were split and dry, and on several fingers had dropped off. The small joints appeared swollen.

On examination.—Vision in the right eye was poor (old keratitis): only able to count fingers. Complete facial paralysis, otherwise nervous system normal. There were small groups of shotty glands in the posterior triangles and in both axillæ.

Blood-count normal. Wassermann reaction negative. Cerebrospinal fluid normal, except for Lange (5555543100). Lymphatic gland—(Guinea-pig inoculation negative). Histological report: An atypical follicular tuberculosis accompanied by marked endothelial cell proliferation. No caseation or amyloid. Sedimentation rate—58 mm. in hour. Mantoux test negative. Skiagrams—Chest: Opacity of lower $\frac{2}{3}$ of right lung with suggestion of cavitation; hands: marked translucency of all bones with a cystic appearance suggesting fibrocystic disease of bone.

Treatment.— $\frac{1}{2}$ c.c. of 3% solution of sodium morrhuate intramuscularly every three days. Ultra-violet light baths twice weekly. Skin lesions had almost disappeared after five weeks' treatment.

Partial Resolution of Leukoplakia Vulvæ under Œstrin Therapy.—

A. D. K. PETERS, B.M., and A. N. MACBETH, M.B.

(I) DR. A. D. K. PETERS

This patient was referred by Professor Fleming to Dr. Brain, who has kindly allowed us to treat and show the case.

She is a married woman, aged 40, who is separated from her husband, works as a waitress and gives the following history.

When 16 years old she menstruated irregularly at intervals of three to six months with one or two days' slight loss and pain on the day preceding menstruation. At 18 she married, had one child at 19, and then three miscarriages. At 25 she was treated for anæmia. At 28 she was menstruating every six months, with bad abdominal pain and pyrexia at the time of each missed period, for which condition the operation of hysterectomy, unilateral oophorectomy and appendicectomy was performed at Montreal in 1925.

She subsequently developed dyspareunia, hot flushes, and irritation of the vulva, perineum, and peri-anal skin. The pruritus has been continuous for the past two years, becoming much worse for the last seven months before treatment. She also complained of frequency of micturition followed by burning pain around the urethra, and of lack of sleep, poor appetite, constipation, and loss of weight.

When seen in February 1937, she was a pale, exhausted-looking woman.

The abdomen showed a median scar. The labia were partially atrophied, the mucosa, perineum, and peri-anal region showed the typical changes of leukoplakia, glistening bluish-white patches and two fissures being present; there was some stenosis of the vagina. The urethral orifice was red and œdematous.

The condition, therefore, corresponded with that described by Adair and Davis as the second phase of chronic atrophic dermatitis of the vulva.

On general examination the heart sounds were faint, pulse-rate 66. Wassermann and Kahn reactions negative. The urine contained no organisms, no albumin, or sugar.

Biopsy from labia.—Sections show hyperkeratinization and flattening of the deep papillary processes. The upper part of the dermis consists of hyaline connective tissue devoid of elastic fibres, and the deeper part is heavily infiltrated with lymphocytes. The appearance resembles that found in the later stages of leukoplakia (D. J. M. Vaux).

Vaginal smear (taken by Professor Fleming after ten weeks' treatment).—Numerous epithelial cells and no leucocytes are present. Bacilli morphologically resembling Döderlein's organism are present in large numbers. Changes are normal for post-puberty pre-menopausal phase (M. V. N. Suds).

Previous treatment had consisted of Sitz baths, sodium bicarbonate lotions, lotio carbol detergens, Dettol cream. 10% silver nitrate, ovarian residue, and a course of daily intramuscular injections of 1 mgm. of œstradiol for a week, followed by 1 mgm. on alternate days for two weeks.

The pruritus had slightly diminished on the last treatment, which was given three months before the present treatment was instituted.

Treatment.—(1) Three intramuscular injections of 5.0 mgm. of œstradiol (50,000 international benzoate units) were given at weekly intervals. The second was followed after two days by pain and enlargement of the breasts and by slight

aggravation of the pruritus. The third was followed by slight improvement of the pruritus and local signs.

(2) One kolpon tablet (containing 0.1 mgm. œstrone=1,000 I.U. with glucose and a buffer substance yielding a pH of 4.5 on solution) was inserted *per vaginam* nightly for two months.

After three days the pruritus became intermittent. The breasts diminished in size and some degree of mammary atrophy returned. After six weeks the hot flushes diminished in frequency and intensity. There was progressive improvement of local signs.

(3) For two further weeks a combined intravaginal and intramuscular therapy was given consisting of 0.1 mgm. of œstrone, in the form of kolpon, nightly, and 5 mgm. of œstradiol benzoate by weekly injections.

In addition thyroid gr. j, radiostoleum m ij t.d.s., and luminal were given at first.

Present condition (after three months' treatment).—Subjectively there is now no pruritus, even on micturition and no hot flushes.

Objectively, there are no visible fissures, the whitish areas are less definite, there is more secretion, the tissues are more elastic and the labia appear to be resuming their normal size and contour. The urethra is less inflamed.

The patient's general condition has remarkably improved; her appetite and hours of sleep have increased.

Commentary.—It is interesting that the most satisfactory method of treatment has been the combination of intravaginal and intramuscular therapy, which agrees with the experience of Davis in treating a group of cases of senile vaginitis. Davis stained biopsy specimens before and after œstrogenic therapy, and so demonstrated that during 6 to 8 weeks the atrophic epithelium had reverted to the normal state associated with active sexual life.

The quantitative dosage is important and also the route of administration. Doubtless intramuscular injections could subsequently be replaced by the oral administration of tablets. The vaginal smear is typical of the high follicular post-menstrual phase described by Papanicolaou.

REFERENCES

- ADAIR, F. L., DAVIS, M. E. (1935), *Surg., Gynec. and Obst.*, **61**, 433.
 DAVIS, M. E. (1935), *Surg., Gynec. and Obst.*, **61**, 680.
 PAPANICOLAOU, G. N., SHORR, E. (1936), *Am. J. Obst. and Gynec.*, **31**, 806.
 BISHOP, P. M. F. (1935), *Guy's Hosp. Gaz.*, **49**, 158.

(II) Dr. A. N. MACBETH

By the courtesy of Dr. Brain and Dr. Peters I was able to see this case after treatment was under way.

It will probably be agreed that the atrophic condition of this woman's external genitalia was causally related to an operation which had removed one ovary and left the other out of commission. Why the external genitalia of this particular patient should have undergone a more profound morphological change than do those of the majority of ovariectomized patients, I am not competent to discuss. (œstrogenic therapy was persisted in because simple or castrational post-menopausal atrophy (an important though probably not the only factor to be considered here) is known to be a reversible process.

The aim of the parenteral œstrogenic therapy has been to supply a sufficient amount of circulating hormone to influence all the tissues susceptible to it. It was hoped that the morphological changes in the vulva would respond adequately to

this alone, but actually the vulvar response seemed to lag behind the mammary response.

The intravaginal therapy followed the observation of many biologists and of the gynaecologists Bernard Zondek [5] and V. B. Green-Armytage [2] that certain hormonal effects are more easily obtained by local application of the hormone (in a form which can be absorbed by the epithelium) than by its parenteral injection. The medium used here consisted of 0.1 mgm. oestrone in each soluble tablet, hence 0.1 mgm. was the daily dose in this instance. It might be expected from the findings of Dobszay [1] that oestrogenic hormone alone would cause the reappearance of glycogen in the epithelial cells and of a lactic ferment in the vaginal secretion resulting in an acidity favourable to the growth of a healthy bacterial flora; but the additional presence in the tablet of a considerable amount of glucose with a phosphate buffer would tend to increase the vaginal secretion and render it acid immediately and before a hormonal effect could be expected; also the dissolved therapeutic media would tend to wash away any dried secretions, whose presence would according to Nabarro [4] delay the epithelial response to oestrogenic stimuli.

Although the human female does not possess an external "sexual skin", highly sensitive to oestrogenic stimuli, as do certain apes, it does not follow that these have no effect on the morphology and vascularity of the skin of the vulva and of the rest of the body. Unpublished observations [6, 3] suggest that the skin is rendered thicker, richer in sebaceous glands, and better vascularized; and that an atrophy of certain elements supervenes after a spontaneous, surgical, or irradiational menopause.

REFERENCES

- 1 DOBSZAY, L. von, *Deutsche med. Wchnschr.*, 1935, **61**, p. 1111; *Zentralbl. f. Gynäk.*, 1936, **60**, 707.
- 2 GREEN-ARMYTAGE, V. B., *Practitioner*, 1937, **138**, 57.
- 3 LOESER, A., Personal Communication, 1937.
- 4 NABARRO, D., and SIGNY, A. G., *Lancet*, 1935 (ii), 604.
- 5 ZONDEK, B., *Schweiz. med. Wchnschr.*, 1935, **65**, 1168.
- 6 ZUCKERMAN, S., Personal Communication, 1936.

Discussion.—Dr. ELIZABETH HUNT said that the diagnosis "leucoplakia vulvæ" was puzzling, because the term seemed to be used indiscriminately for whitish lesions occurring on the normal skin of parts adjacent to the vulva, as well as for lesions on the vulva itself, whilst in dermatological textbooks the term "leucoplakia" was restricted to lesions of mucous membrane only.

The present case showed lichenification of the perineum and some small hyperkeratotic patches on the internal surfaces of the labia majora, and would probably be classified by German authors as a case of kraurosis vulvæ.

The histology of leucoplakia vulvæ had been first demonstrated by Mr. Victor Bonney, and in a recent article¹ she (the speaker) had shown that Mr. Bonney had in effect demonstrated the histology of lichen planus, and that in a large number of cases leucoplakic lesions of the vulva and adjacent surfaces were associated with lesions of lichen planus at other sites.

With regard to treatment of vulval skin affections with oestrin: it had been shown experimentally that oestrogens produced a specific effect on the epithelium of the reproductive organs, in the female on those derived from the Mullerian ducts, the uterus and the vagina, in the male on those derived from the urogenital sinus.

That small area of the vulva lying between the labia minora, and known as the vestibule, represented the vestigial remains of the urogenital sinus in the female, but skin affections of the vulva were rarely limited to this area only.

In the present case this area looked moist, but she (Dr. Hunt) could not see regeneration of other parts, namely of the stunted labia minora and the lichenified perineum.

She thought that the administration of oestrogens for skin affections of the vulva was fraught with the risk of overdosage to obtain results, and that repeated administration, which

¹ *Brit. J. Dermat.*, 1936, **48**, 53.

was necessary owing to reversion to the original state on withdrawal, might prove carcinogenic in some cases.

She did not advise oestrin therapy because she found that equally good results were obtainable with other therapeutic measures, the administration of which could be repeated without any risk to the patient.

Dr. AGNES SAVILL said that for nearly ten years she had been treating cases of kraurosis by local diathermy, according to the method introduced by Dr. Cumberbatch, who had used it successfully for menopausal arthritis; his conclusion was that it must act by stimulating ovarian secretion. She had tried it first empirically in a case of definite kraurosis vulvæ—in a patient aged 66, into whose vulva it had been impossible to introduce an ordinary writing pencil. After twelve treatments the condition had totally changed; when seen two years later a large speculum had been introduced easily. She (Dr. Savill) had had several equally successful cases, and now had under observation a woman aged 77, who had been in a bad state when she had come four years previously, because she did not respond to radium. To diathermy, however, she had responded quickly. She had from time to time little fissures, but occasionally-used diathermy kept her so well that she had arranged to have a few doses twice or thrice a year. Nothing was used locally except almond oil. She (Dr. Savill) would be afraid to employ oestrin, but there was no danger in diathermy.

Dr. W. FREUDENTHAL said that Werner Jadassohn had just published a paper in which he proved in animal experiments that a folliculin ointment produced a local but also hæmatogenous specific effect.

Various conditions might appear clinically as leukoplakia, e.g. a case the sections of which were shown to him by Dr. Hunt was in his opinion histologically one of lichen sclerosis.

The PRESIDENT said that the important point was the diagnosis; he had not examined this patient. He agreed with Dr. Hunt that many of the cases called leukoplakia were really lichen planus; they must be distinguished from those of true kraurosis vulvæ. The latter should respond to oestrin therapy.

Dr. PETERS (in reply) said that with reference to the diagnosis, Traussig's views had been followed. The lesions, their distribution, and microscopic appearance seemed to be typical of leukoplakia vulvæ. Traussig restricted the use of the term "kraurosis" to the symptoms of narrowing of the vaginal outlet by sclerosis of the vulval ring. This frequently occurred in the later stages of leukoplakia vulvæ, and in this sense this case might be described as being one of leukoplakic kraurosis.

Davis suggested that the symptoms of burning and pruritis and the anatomical changes might be due to the effect of trauma and infection upon an inelastic and physiologically atrophied epithelium. Doubtless these were important factors, even if they might not be the only ones.

[June 17, 1937]

Superficial Cicatrizing Rodent Ulcer of the Left Upper Eyelid.— ELIZABETH HUNT, M.D.

The patient, a woman aged 32, says that she had a birthmark on the side of the nose which "scaled" about twice a year for many years. For two years before she came for treatment this had been increasing in size and in the last year it had bled at times.

When seen, this lesion looked like a rodent ulcer, with a depressed centre covered with a scale, and a raised pearly-looking border. It was treated with radium and ulceration followed, but the lesion still shows a typical rodent ulcer border on the inner side, which has not been destroyed.

Over the adjacent surface of the eyelid is another lesion which has not been treated. It is about $\frac{1}{2}$ cm. in width, has a smooth, slightly atrophic-looking, centre, surrounded by a curious white threadlike beaded border, which is continuous with the border round the rodent ulcer on the nose, forming with it a figure-of-8 on its side.

Dr. R. T. BRAIN agreed that the lesion was probably a superficial rodent ulcer. In the lesion nearest the nose there was a definite raised, and somewhat pearly, edge. The adjacent unusual lesion was probably of the same type.

Poikiloderma with Acrosclerosis and Muscular Wasting.—H. C. SEMON, M.D.

G. M., a married woman aged 24.

History.—Was treated four years ago at University College Hospital by Sir Thomas Lewis for Raynaud's syndrome of the upper extremities.

Two years ago she began to notice increasing fatigue and, concomitantly, loss of the eyebrows and eyelashes.

One year ago the first signs of skin irritation and rash on the face, neck, and upper part of the back appeared.

In February of this year the scalp hair began to fall out, and the patient noticed stiffness of the feet which rendered walking difficult. A small ulcer developed on the inner side of the left ankle, resisted all attempts to heal, and brought her to the Royal Northern Hospital out-patient department, from which she was admitted as in-patient on 26.5.37.

Past history.—Miscarriage in March last. No other significant point elicited.

Examination.—Cardiovascular, renal, and central nervous systems: nothing abnormal detected. There is general wasting of the musculature, both of limbs and trunk. The patient rises from the supine position with difficulty, and sometimes finds it difficult to keep her head from falling back on the pillow. She tends to lose her voice after speaking for any length of time. There are no abnormal reactions either to faradism or galvanic make-and-break. An X-ray photograph of the chest did not reveal any organic disease, and radiograms of the hands and fingers were normal.

There are striking and characteristic alterations in the skin, and its appendages.

The face is pinched in appearance, and has but little expression, although the patient's mentality is cheerful and intelligent. There is complete loss of the eyebrows and eyelashes, and on the scalp there is marked denudation especially over the left parietal region where the skin appears to be thin and atrophic to palpation. There is slight branny scaling on the cheeks and chin, with considerable cutaneous atrophy over the nasal and aural cartilages. On the neck and upper part of the trunk, back and front, the skin presents the mottled and variegated changes termed poikiloderma, with telangiectases and shifting of the pigment. Similar, though less marked, changes are apparent on the lower abdomen and thighs. The fingers are tapered towards their extremities, and the terminal phalanges of the indices are hard to the touch, the skin being bound down to the underlying tissue. This apparent "sclerosis" is sufficient to prevent fist closure, and is much more evident over the dorsa of the feet, where the epidermis is tightly bound down so that it cannot be lifted off the underlying fascia and tendons. The progress of the affection has resulted in an increasing difficulty in walking, and is doubtless responsible for the trophic ulcer which has developed over the left internal malleolus.

A consideration of the history and development of symptoms in this case suggests a rather close analogy with the precepts laid down by J. Selli of Budapest for the condition termed by him acrosclerosis (*Brit. J. Dermat.*, 1934, 46, 528-532). Briefly these include:—

- (1) Simultaneous origin of the disease on the hands (or the feet), and on the face at the same time.
- (2) Changes strictly symmetrical.
- (3) Vasomotor symptoms of the Raynaud type.

(4) Certain subjective symptoms—e.g. pains in cold weather.

(5) Trophic changes due to shrinkage on the hands and fingers and on the toes, leaving star-like scars on the finger-tips which become tapered, as in my case. The face becomes mask-like and taut and there may be a certain rigidity to the touch—a point which is very definitely present over the mastoid processes and on the insteps and dorsa of both feet in this patient.

(6) Ulnar adduction—not present here. Hardening of finger-tips—a process which differs in certain respects from a true sclerodactylia in which the sclerosis advances from above downwards.

(7) The mask face above mentioned, with shrinking of the nasal skin (auricular skin in my case) and protrusion of the teeth, also present in some degree in my case.

(8) Very frequently, telangiectasia on the face and trunk. Is this the poikiloderma present in my case?

While the above description tallies generally with the history and present state of my patient it differs in one very important particular, namely the absence of any mention of muscular wasting which is here so pronounced a feature and which seems to place this among the poikiloderma-myositis cases (Petges' type), except for the fact that a histological examination of the muscle did not reveal the characteristic changes described in that condition, while the creatinine ratio in the urine is also normal.

In many respects this case resembles that described, in 1934, by Ingram and Stewart.

Discussion.—Dr. W. N. GOLDSMITH asked whether the patient showed any sign of muscular weakness, as distinct from loss of muscle volume.

Dr. F. PARKES WEBER said he did not see why this condition should not be regarded as true sclerodactylia. Muscular wasting might accompany sclerodactylia (the latter being a more or less generalized and symmetrical form of scleroderma, according to the old classification). Raynaud's symptoms (as in the present case) occurred in at least 60% of cases of sclerodactylia. This patient also had a very marked telangiectatic change, which was a pronounced feature in some cases of generalized scleroderma. It was possible that in some cases the muscular weakness was allied to myasthenia gravis, rather than to myositis (as in poikiloderma myositis).

He did not see any reason for changing the nomenclature and speaking of acrosclerosis.

The PRESIDENT said that he had approached the case with the preconceived idea that it was sclerodactylia, but the point against what Dr. Parkes Weber had just said was that there was no sclerodactylia of the fingers. He agreed with Dr. Semon that in certain areas the patient had atrophy and telangiectasia.

Dr. PARKES WEBER said that the present patient's feet showed sclerodactylia strikingly, involving not only the toes but the whole feet. But atrophodermic changes might take the place of a typical sclerodermic condition.

Dr. SEMON (in reply) said that muscular weakness was a very marked feature of the case, so much so that if the patient sat up in bed for any considerable time her head fell back, and it was necessary to adjust pillows to prevent it. In the clinical history easy fatigability was one of the striking features. He asked whether Dr. Parkes Weber eliminated Sellei's observations descriptive of acrosclerosis, urging that the old terms sclerodactylia and scleroderma should be adhered to. Sellei¹ had tried to separate out two clinical groups, emphasizing the clinical difference between scleroderma and acrosclerosis. Did Dr. Weber agree there were these two separate diseases?

Dr. F. PARKES WEBER (replying to Dr. Semon) said he regarded the diseases mentioned not as separate diseases but as different types. There were many types, some involving

¹ Sellei, J., "The Diagnosis and Treatment of Scleroderma and Acrosclerosis and Some of Their Kindred Diseases", *Brit. J. Dermat.*, 1934, **46**, 523.

muscle, of sclerodermia and morphœic sclerodermia. He remembered the case of a woman in whom a myasthenic condition of the neck muscles was present with sclerodermia (cf. F. P. Weber and O. B. Bode, *Proc. Roy. Soc. Med.*, 1932, 25, 966), and in the present case the muscular trouble might be myasthenic more than atrophic.

Dr. C. H. WHITTLE asked whether such cases as this would be likely to respond to prostigmin, and if so whether it should be given orally or by inoculation.

Dr. PARKES WEBER (in reply) said that in the case which he had mentioned the myasthenic feature was hardly troublesome enough for a trial of the treatment in question.

Fox-Fordyce Disease.—R. T. BRAIN, M.D.

The patient is a married woman aged 27.

History.—For two or three years there has been a papular eruption in the axillæ; the lesions irritate when the patient is excited or tired.

Onset of catamenia at 12 years of age; regular; lasting seven days.

Has 1 child, aged 6½ years, healthy. Now 20 weeks' pregnant. Spots have been rather less irritable during the pregnancy. Boils on face only.

On examination.—Healthy woman. Numerous pale pink or normal skin-coloured shiny dome-shaped papules in both axillæ. Rather uniform in size (approximately 0.3 cm. in diameter).

Dr. F. PARKES WEBER said that this reminded him of a case in which a biopsy had been carried out. The patient was a young woman who had minute nodules aggregated in the axillæ, with scarcely any itching or any kind of paræsthesia. Dr. Freudenthal's microscopic examination had shown that the lesions were cysts—one form of sebocystomatosis. The present patient had had practically no itching, and he (Dr. Weber) wondered whether the axillary lesions were not cysts of the same kind.

Chronic Granulomata.—HUGH GORDON, M.C., M.R.C.P.

The patient, a healthy woman aged 56, eight months ago had what appeared to be an indolent boil on the right leg. This was fomented; it discharged but failed to heal, and formed a septic-looking sore. Since that date other lesions have appeared on the legs, back, and chest.

When first seen six weeks ago, there were six circumscribed lesions on the right leg and three on the left, all about 1 in. in diameter. The surface was bluish granulation tissue with here and there "honeycombs" filled with pus. The skin at the circumference was not reddened. The lesions were quite indolent and not painful. On the back was the most recent—a bluish fluctuant swelling suggestive of a gumma on the point of bursting.

The Wassermann reaction was negative, but definite improvement followed the first two injections of novarsenobillon. Progress after the third injection was negligible and the patient was admitted to hospital for further investigation.

One lesion on the right leg was removed for bacteriological and pathological examination; the result was negative. Pathologically there is no evidence of mycosis fungoides, blastomycosis, or sporotrichosis; the appearance is that of an infective granuloma. Puncture from the unopened swelling on the back yielded a poor growth of *Staphylococcus aureus*. The blood-count is normal.

Treatment has been three further injections of novarsenobillon—each of which has been followed by a slight pyrexial reaction—and instillation of liquid permyase, hypodermically. The lesions on the outer side of the left leg had a test exposure ten days ago of one pastille dose of X-ray (unfiltered); these alone have now a red areola. The beneficial result has been slight. The lesions have all steadily progressed and are all flatter and much less purulent than they were on admission.

Dermatomyositis: ? Artefact.—HUGH GORDON, M.C., M.R.C.P.

The patient a previously healthy woman aged 23, was first seen in February 1937, having what appeared to be an acute dermatitis of the face; no cause was found for this and she was treated on symptomatic lines. The dermatitis, however, persisted. It was sharply marginated, running in a straight line across the bridge of the nose and the cheeks. It did not respond to treatment.

After six weeks a symmetrical erythematous patch appeared on the outer side of both upper arms. There was no vesiculation, scaling, or irritation. The diagnosis of an early poikiloderma or dermatomyositis was considered. A biopsy of a piece taken from the left arm showed no pathological changes.

Under observation in the out-patient department the three fixed erythematous patches faded, but showed signs of pigmentation and reticulation suggestive of poikiloderma which was considered the probable diagnosis.

A month ago the patient's general health was said to be worse and she complained of giddiness and general weakness. About that time the face became covered with small erosions which gave it a blood-stained appearance. These looked like a classical artefact. On examination she was found to have a symmetrical streaky pigmented red erythematous patch on the inner side of each breast. This appeared about the same time as the patches on the arms. There is no doubt as to the patient's extremely neuropathic make-up; apparently many factors in her recent psychological history have greatly aggravated it. The erosions and blood-staining are, I think, definitely artefacts. On the other hand, during the last week the lesions on the upper arm have become bright red and appear to be swollen. Extreme tenderness is complained of, but the reality of this is difficult to assess.

Hand-grip is poor, as also are muscular movements. This observation, again, in view of the hysterical element, is of doubtful value.

The case does, however, appear to conform to a diagnosis of dermatomyositis. The lesions are so definitely fixed and are so subject to acute exacerbations of tenderness and increased redness, that it seems impossible to account for them satisfactorily by a diagnosis of simple artefact. A biopsy of muscle will shortly be carried out.

Lupus Vulgaris with Cutaneous Horns.—A. WILLCOX, M.B., M.R.C.P. (for H. MACCORMAC, C.B.E., M.D.)

R. L., a man aged 37.

History.—A large hæmangioma has been present over the right temporal region since birth. The patient says that he was first treated for lupus vulgaris of the right cheek and ear at the age of four years, at which time he also had tuberculosis of the left hip-joint. When he was ten years old the affected area on the right cheek was excised and a skin-graft was applied. He was treated by ultra-violet light at the Middlesex Hospital for the next twelve years. He then ceased to attend and for the last fifteen years has received no treatment. The lupus began to spread over the right cheek soon after he ceased having treatment, growth being most pronounced in the winter months. Two years ago two cutaneous horns appeared on the right cheek at about the site of the original lesion which had been excised. They also have grown particularly in the winter months and have become smaller in the summer.

Present condition.—There is a hæmangioma extending over the temporal region of the right cheek and forehead. There is an extensive area of lupus vulgaris on the right side of the face, about 4 in. in diameter, spreading across the cheek to the margin of the naevus, involving and deforming the ear, extending up into the scalp and down to the neck about the angle of the jaw. Around the ear it is atrophic, with scar

tissue containing apple-jelly nodules. Two cutaneous horns are present on the right cheek. They arise from a common base, where the area of lupus impinges on the naevus. One is 2 in. long, the other 1 in. The lupus at their base is rather hypertrophic and suggests the possibility of an underlying epithelioma.



Case of lupus vulgaris with cutaneous horns.

Dr. W. N. GOLDSMITH said that he had seen a case of lupus vulgaris in which there were long, thin, horny processes more diffusely distributed. They had persisted for a long time without developing any malignant changes. He did not think the horny overgrowth in the present case necessarily indicated epithelioma.

? Acne Conglobata.—F. A. E. SILCOCK, M.D.

Patient, a man aged 34, a confectioner, says that his health has been good, except for the present skin trouble. He had a slight accident to his lumbar spine when six years old and was treated at Northampton General Hospital. Both parents are alive and well; four brothers and three sisters are all alive and healthy. He has never been out of England.

History of present complaint.—The lesions under both armpits began "like an abscess" eight years ago. They were incised by his local doctor and pus was evacuated. The affected areas have gradually spread. The skin over the posterior aspect of the left buttock became swollen; it was incised and pus was found, four years ago. Since then it has spread on to the skin of the right buttock and down the upper half of the left thigh posteriorly, and is now extending into both groin

folds anteriorly. The condition is painful on the buttocks, but the armpits do not now trouble the patient much.

Present condition.—Thin and pale. General condition poor. No pyrexia. No signs of comedones or acne vulgaris on body or face. Wassermann reaction negative. Chest normal, clinically and radiologically. No enlargement of lymphatics, and all other organs, &c., normal.

Left axilla: There is an atrophic-looking scar, over which the skin appears to have been superficially ulcerated, extending five inches vertically and four inches



FIG. 1.—Acne conglobata—Bridge-like scars (Brückennarben) of Lang. A paper arrow marks the opening of one and a piece of gauze is inserted beneath the other.

horizontally across the widest part, involving the chest wall and upper part of the arm. It is bounded below by a circinate, unhealthy, heaped-up, granulomatous-looking edge, from which a little pus exudes in places. On the side of the chest wall over the area affected there is a vertical pedicle of hard fibrous tissue $\frac{1}{4}$ in. in diameter, covered with normal skin and extending for 2 in. along the chest wall; this is attached at both ends only and is free in the middle along practically its whole length. There is another firm, fibrous-like band $\frac{3}{4}$ in. in diameter across its widest part, extending horizontally across the apex of the axilla, and in one part there is a complete through and through opening behind this tuck-like affair. (Fig. 1. In the

photograph a piece of gauze is shown inserted behind the former band of tissue and a paper arrow with its point inserted through the opening of the latter one.)

Right axilla : A somewhat similar condition to that on the other side is present, but here it spreads more on to the skin of the inner side on the upper arm, and there is no vertical pedicle present. There is another marked horizontal fibrous band, or tuck, 3 in. in length and about the same diameter as on the other side, at the apex



FIG. 2.—Acne conglobata—Lesions on buttocks; undermining abscess formation; numerous discharging sinuses and small ulcers.

of this axilla ; it has no through opening however, but the skin behind it is only very thin and no doubt would readily break down with slight sepsis.

Buttocks : The skin over both these posteriorly is bluish-purple in colour, undermined and unhealthy looking, with the openings of numerous fistulæ and sinuses present, giving it a crateriform appearance (fig. 2). Many of these fistulæ intercommunicate and allow the free passage of a probe from one to another. (The general look of the skin here closely resembles that of a tuberculoderma or scrofuloderma, on first sight.) The skin condition extends down the upper half of the left thigh posteriorly and is advancing into both groin folds, involving the

scrotal-groin folds where it is tending to form similar tuck-like bands to those in the axillary apices.

The pus from the buttocks is crowded with polymorphonuclear pus cells and many different kinds of organisms, both cocci and bacilli, Gram-negative and Gram-positive. Large numbers of spirilla present. Culture: crowded with *Staphylococcus aureus*; no other organisms.

Progress.—Since the patient was admitted into hospital twelve days ago the general sepsis of the affected skin has much decreased under treatment by saline baths, saline and paraffin soaks, &c., locally.

Comment.—These cases are apparently rare, and dermatologists seem to vary in their clinical interpretation of the signs, &c., of this disease. I have looked up in the *Archives of Dermatology and Syphilis*, 1931, 23, 49, an article by Drs. H. F. Michelson and P. E. Allen, and I think this case fits in with their description of acne conglobata. They describe it as often leaving keloidal or so-called bridge scars (Brückennarben) of Lang. This case is a very marked example of these.

Discussion.—The PRESIDENT said he thought that this case belonged to the group acne conglobata, though to him the term seemed an unsuitable one for the disease. He had had a characteristic case of it in a man who eventually died. He asked whether Dr. Silcock had found acid-fast bacilli, as he understood that in the case shown by Dr. A. M. H. Gray,¹ there had been enormous numbers of acid-fast bacilli, which were not, however, tubercle bacilli.

Dr. F. PARKES WEBER said he thought the appearance of the disease was due to the chronic spreading suppuration in the panniculus adiposus about the lesions of the acne conglobata. But in the present case the lesions were deeper and more extreme than those in the older case illustrated. One could not imagine an ordinary phlegmon gradually spreading and lasting so long. In very rare cases of a variety of acne on the back there were undermined scars—a kind of miniature of what had occurred in the present case.

Dr. R. KLABER said that from two of his cases of acne conglobata Dr. Garrod had obtained pure anaerobic cultures of a small Gram-negative bacillus. This organism had not been identified with any known variety. The preparation of anaerobic cultures from these cases might be worth the attention of other investigators.

Dr. C. H. WHITTLE suggested that this was a staphylococcal infection. He had seen one case of furunculosis of the buttock, in which the lesion spread to give a similar curious, extensive, very thick œdematous red mass, with the rabbit-warren condition underneath. Clearly it was at first a case of boils, which then went on to a condition looking much like that in the present case. It was very intractable and had persisted for eighteen months, but eventually it was cured. A toxoid was used in treatment, and it might be well to use a staphylococcal toxoid in the present case. It was difficult to bring the axillary lesions into line with the condition on the buttocks.

Dr. SILCOCK (in reply) said he noted that the President considered the term "acne conglobata" unsatisfactory. There were no signs of acne anywhere else in this case, and he had put a query mark before the title. He would be grateful for suggestions as to treatment. The pedicles could be dealt with by "spring-cleaning" with the knife. It might be of use to try to get an organism from an unopened lesion. The patient had been in hospital only a few days, otherwise a more extended investigation would have been carried out.

Nail Dystrophy (Onychomadesis).—F. SHERRY-DOTTRIDGE, M.B.

The patient, a woman aged 29, had normal nails until three years ago, when they gradually thickened and became loose. Now all the finger-nails are rounded, yellowish, and much thickened, and are separating from the matrix from the distal ends. Both thumb-nails have been shed in one piece and all the others are separating. The toe-nails show a similar condition in a lesser degree.

¹ *Proc. Roy. Soc. Med.*, 1931, 24, 1013 (Sect. Derm., 45).

Teeth and hair normal. Wassermann reaction negative.

Past history.—Right mastoidectomy, 1935; bilateral antrostomy, 1936; bronchiectasis diagnosed and confirmed by lipiodol X-ray examination, 1936.

(I have to thank Dr. R. T. Brain for permission to show the case.)

Dr. F. PARKES WEBER said this seemed to be a case for trying general treatment. He wondered whether the patient had a mild achlorhydric anæmia; that would give some clue in regard to general treatment.

Section of Obstetrics and Gynaecology

President—CLIFFORD WHITE, F.R.C.S.

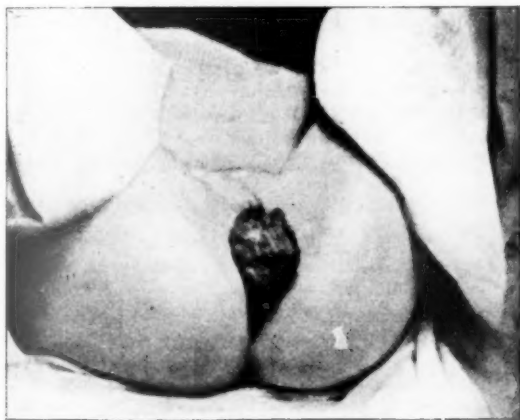
[June 18, 1937]

**Two Cases of Carcinoma of the Cervix complicating
Procidentia Uteri**

By T. F. TODD, M.S.

THE rarity of carcinoma of the cervix associated with complete uterine prolapse is one of the most striking contrary findings to the commonly accepted theory that chronic irritation is an important aetiological factor in the genesis of cancer. Procidentia uteri is common, yet there are less than forty cases of procidentia with superimposed cancer reported in the literature. I have treated two such cases recently, and I thought them worth recording, in view of their rarity.

I.—The first occurred in a 6-para aged 41, spontaneously delivered of a full-term child in October 1934. During the last six weeks of her pregnancy she complained of intermittent vaginal hæmorrhage, but this was made light of at the clinic she attended. Following delivery hæmorrhage persisted more or less continuously until August 1935 when I first saw her. She then had a complete procidentia with a massive proliferating growth covering the whole of the cervix, and extending well along the vaginal wall on the left side. Biopsy showed the growth to be a non-keratinizing epithelioma.



Carcinoma of the cervix complicating procidentia uteri. Case I.

Attempts at reduction under anaesthesia failed, so vaginal pan-hysterectomy was performed. Convalescence was uneventful, and in three weeks' time a "sorbo" ball 4 cm. in diameter, and containing 27 mgm. of radium, was sewn into the vagina and left there for six days; this was followed by a course of deep X-ray therapy—approximately 3,000 R. units being delivered to the cervical region through five fields over three weeks. The patient tolerated treatment well and was discharged reacting normally. She failed to attend the follow-up clinic, and was not seen again.

until nine months afterwards, when she was readmitted because of abdominal pain and backache. She was found to have a tumour mass in the abdomen to the left of the navel; presumably a metastasis in the lumbar glands. The vagina was stenosed, but rectal examination failed to reveal any sign of malignancy in the pelvis. The patient went down-hill and died eleven months after operation. Permission for autopsy was refused.

This case demonstrates one of the limitations of both vaginal hysterectomy and pelvic radiation, namely when glandular metastasis has already occurred. Perhaps the story would have been different had a speculum examination been made when the patient complained of bleeding ante-natally. Surely a visual examination is as important during pregnancy as at any other time!

II.—The second case occurred in a 2-para aged 62 who had had a complete prolapse for twelve years. A ring pessary had been used intermittently without success. For several months the prolapsed mucosa had been ulcerated and was causing a foul discharge. I saw her first in December 1934 when there was extensive superficial ulceration of the whole of the upper half of the posterior wall of the vagina extending to the margin of the external os. Biopsy showed a keratinizing squamous epithelioma.

The prolapse was easily reducible in this patient, so that surgery was not necessary. A "sorbo" ball 5 cm. in diameter and containing 34 mgm. of radium was stitched into the vagina and left in situ for eight days. No other treatment was given—the patient was too obese for treatment by deep X-rays. The local lesion cleared away in a month and there has been no recurrence since. The whole uterus still prolapses on the slightest effort, but is easily reducible, and I have seriously contemplated advising a Le Fort operation.

In spite of birth trauma and chronic irritation malignancy rarely supervenes on procidentia. I have no new theory to offer as regards the explanation of this phenomenon. Haegler (1933) considers it an argument against the generally accepted one of chronic irritation being the causative factor in the development of cancer. Tourneux (1934) finds none of the theories advanced satisfactory. Emmert and Taussig (1934) are of the opinion that if all decubitus ulcers were routinely biopsied several more cases would probably be discovered. A compact summary of the literature, and the report of another case treated by vaginal hysterectomy is given by Brady (1935).

REFERENCES

- HAEGLER, H. (1933), *Arch. f. Gynäk.*, **150**, 135.
TOURNEUX, J. P. (1934), *Gynécologie*, **33**, 273.
EMMERT, F. V., and TAUSSIG, J. B. (1934), *Am. J. Obst. and Gynec.*, **28**, 521.
BRADY, L. (1935), *Am. J. Obst. and Gynec.*, **30**, 277.

Procidentia Recti Present for Twenty-three Years and Cured by Operation

By T. F. TODD, M.S.

WHEN I first saw this patient I was reminded of "Mother India", and she might well have been described by Katherine Mayo. She was aged 43, and a 6-para, and she was referred to me on account of uterine prolapse. Her story was that immediately following the spontaneous birth of her first child, twenty-three years previously, the swelling in the perineum had appeared, and had persisted since. She had never had any bowel trouble, melæna, or menstrual abnormality. The swelling had never gone back, and in each of her subsequent confinements it had been mistaken by the

midwife in attendance for the foetal head—to the patient's amusement, and the midwife's discomfiture!

On examination she was found to have a large fleshy tumour between her legs, appearing from the vulva. The mass was about the size of a heavy-weight boxer's hand and fist—appreciably larger than the usual procidentia uteri. On close inspection the mass was seen to be issuing from the anus, not from the vagina. The vaginal introitus was normal, and there was no descensus uteri—in fact her six confinements had caused the minimum of damage to the genital tract. The mass was, in fact, a procidentia recti. There was no mucosal ulceration, which was surprising, as she was hardly a cleanly person. Elsewhere there was no sign of disease or abnormality.

I advised her to have the prolapsed rectum removed. She was carefully prepared for two weeks, and then given a spinal anaesthetic, under which it was possible to reduce the mass, though it prolapsed through the patulous anus immediately my fingers were removed. It seemed, in consequence, an unsuitable case for any of the more complicated operative procedures, so I excised the whole tumour at the anal margin. The peritoneum was necessarily opened, but no intestine was prolapsed. A series of fourteen mattress sutures approximated the periphery of the uppermost part of the rectum to the anal margin. On completion it was possible to introduce four fingers into the anus without difficulty, and I visualized the possibility of having to perform a subsequent tightening of the sphincter. However, the patient made an excellent recovery, and within three weeks had almost complete control over her bowel action. When she was re-examined four months after her discharge from hospital the anus appeared quite normal and would admit only one finger without discomfort. The patient had complete control over her bowel action, and was very pleased with the result; there was no suggestion of any tendency to recurrence on straining or coughing.

Results of Radium Treatment in (1) Carcinoma of the Uterus ; (2) Uterine Hæmorrhage

By DAME LOUISE McILROY, D.B.E., M.D.

(1) IN CARCINOMA OF THE UTERUS

Most gynaecological surgeons have now accepted radium therapy as an established method of treatment of carcinoma of the uterus and it is hoped that the days of doubt and controversy are over. For early cases of carcinoma the choice lies between hysterectomy and radium. I do not attempt to discuss the relative merits of X-rays as I have had so little experience of the results, but as a follow-up of surgical or radium treatment they have an important place.

The results of surgery and radium can never be made comparable in unselected cases. Hysterectomy is only possible in a limited number of cases—those which come for treatment in the early stages of the disease. In my 95 cases of carcinoma of the cervix treated by radium, only 5.3% were in the early stages (Type I); that means that operation would in all probability be completely successful: 24.2% were doubtfully operable, belonging to Type II. At the best this gives an operable rate of 29.5%. The remaining 70.5% were doomed to death within two years if radium had not been used. Surgery therefore is limited to selected cases. Radium treats unselected cases with the exception of the very hopeless conditions in which its application would only hasten the end.

Are the results of any method of treatment of carcinoma very successful as a whole? If good results are obtained by radium in borderline cases, then it stands to reason

that these results will be much better in early cases. In advanced cases radium prolongs life, makes it more bearable, and takes away the offensive discharge which is the bane of the dying patient.

In the majority of my patients the disease was fairly advanced and there was little choice in the method of treatment, although it is now my practice to treat all cases of carcinoma of the cervix with radium. The results are published for the first time and extend over nearly ten years. I fully realize that these results are open to criticism in that in some cases the duration of time from the application of radium has not come up to the 5 to 10 years standard, but I have endeavoured to give all the results as they were treated. With very few exceptions the patients have been examined by me at regular intervals as long as they survive, and I am much indebted to the administrative staff of the Marie Curie Hospital for keeping the records of these attendances.

The majority of the patients were treated in the Marie Curie Hospital. A few were treated in the Royal Free Hospital. The success of the results is due to the team system in the Marie Curie Hospital and to the supervision by Dr. E. Hurdon of every patient treated by the surgeons on the staff. I am indebted to Dr. Gilmour, the pathologist, for the use of the microscope slides, and to Mr. Gye for permission to have the photomicrographs prepared in his laboratory.

Radium therapy has its dangers unless it is carried out in the hands of experienced workers, and good results are obtained only by the co-operation of physicist, pathologist and surgeon. The haphazard methods of isolated workers tend to bring radium into disrepute.

In every case a microscopical examination of the endometrium was made and in cases of suspected disease of the cervix a wedge was removed for examination. This procedure confirms the diagnosis and the character of the growth. In cases of uterine hæmorrhage in which carcinoma has been suspected and is found to be absent the biopsy gives the patient great peace of mind.

Two examples illustrate this statement. A patient aged 70 had a clinical diagnosis of scirrhus of the cervix. The biopsy gave negative results. The Wassermann reaction was positive and with treatment the uterine hæmorrhage was completely cured. A patient aged 76 had had irregular hæmorrhage for three years; no carcinoma was found. A single dose of radium in the cavity of the uterus cured the condition.

The method of application of radium is based on that of the Radiumhemmet in Stockholm, with modifications suggested by Dr. Hurdon and the late Dr. Helen Chambers. The details of treatment were published in 1929 by the Marie Curie Hospital ("The Radium Treatment of Cancer of the Uterus", London).

The method of application is as follows:—

For carcinoma of the cervix (fig. 1).—Intra-uterine applicators each containing 25 mgm. radium element, screened in 1 mm. platinum. Both tubes enclosed in a rubber tube whose end slightly projects at the os.

Three vaginal applicators each containing 20 mgm. radium element (5 small tubes of 4 mgm. each; platinum screen 1.3 mm., enclosed in silver box of 2 mm. thickness and covered with rubber). Kept in position by gauze soaked in acriflavine (1 : 2,000).

First application : 120 mgm. for twenty-two hours ; second application 120 mgm. for twenty-two hours ; third application 120 mgm. for twenty-two hours.

For carcinoma of the corpus (fig. 2).—Three small intra-uterine applicators, containing 8 mgm. radium element. Two larger applicators containing 25 mgm. radium element ; platinum screen 1 mm., rubber tubing ; silver wire tags are used.

Two vaginal applicators containing 20 or 25 mgm. radium element, platinum screen 1.3 mm., silver box 2 mm., rubber covers. Kept in position by gauze soaked in acriflavine (1 : 2,000).

First and second applications 124 mgm. radium element for twenty-two hours.
Third application intra-uterine only for twenty-two hours.

Minor modifications of these applications are made for individual cases.

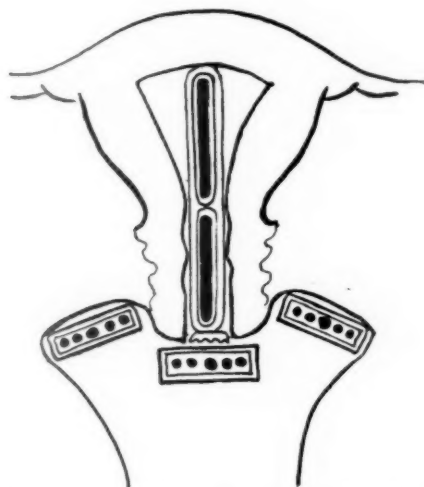


FIG. 1.—Radium applicators in situ; carcinoma cervicis.

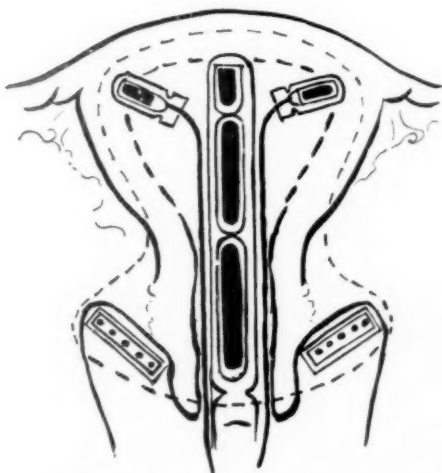


FIG. 2.—Radium applicators in situ; carcinoma corporis.

Number of cases.—Carcinoma of cervix 95; carcinoma of corpus 18; total, 113.

CLASSIFICATION OF CARCINOMA OF CERVIX UTERI.

95 cases.				Cases	Per cent.
Type I.	Early, operable, cervix only	5	5.2
Type II.	Borderline, growth in adjacent tissues but no fixation of uterus	24	25.2
Type III.	Inoperable, invasion of rectum, vagina or septæ of uterus. Broad ligaments involved	49	51.7
Type IV.	Advanced. Pelvic block. Hopeless	17	17.9
Total				95	100.0

Comparative survival and mortality rate of types.

Total survival rate—31.9 per cent. in 95 cases.

Type	Cases	Per cent.	Survival Per cent.	Mortality Per cent.
I	5	5.2	80.0	20.0
II	24	25.2	62.5	37.5
III	49	51.7	30.7	69.3
IV	17	17.9	5.9	94.1

Result to patients in each year group.

Type I.—5 cases.

Year group	Alive	Dead
2—3	0	1
5—6	1	0
6—7	1	0
7—8	1	0
8—9	1	0

Survival rate = 80 per cent.

Type II.—24 cases.

Year group	Alive	Dead
1—2	2	5
2—4	5	4
4—6	4	0
6—7	1	0
8—9	2	0
9—10	1	0

Survival rate = 62.5 per cent.

Type III.—49 cases.

Year group	Alive	Dead
1—2	3	27
2—4	3	7
4—6	4	0
6—7	1	0
7—8	3	0
8—9	1	0

Survival rate = 30.7 per cent.

Type IV.—17 cases.

Year group	Alive	Dead
1	0	11
1—2	0	4
2—3	0	1
4—5	1	0

Survival rate = 5.9 per cent.

Pre-menopause cases 18.9% ; at menopause 21.1% ; post-menopause 60.0%. Average age, 51 years 10 months. Youngest patient 27 years ; oldest patient 76 years. One patient was unmarried, six were married, but nulliparous, 18 had two children, 56 had three children or more. Over 50% had histories of difficult labours or discharges subsequently. The total mortality due to recurrence was 57.8% and that due to other factors was 5.2%. All the patients had squamous carcinoma of the cervix.

Two cases are of especial interest:—

(1) Patient aged 36, multipara 5. Seen, when fourteen weeks' pregnant, with early carcinoma of the cervix. Radium was applied three times in the vagina; abortion occurred after the third dose. A rectal fistula developed. Treatment was carried out eight years ago and the patient has had no recurrence.

(2) Patient aged 49. Carcinoma of the cervix was found on examination. Eight years previously a sub-total hysterectomy had been performed for fibroids. Three modified doses of radium were given. The patient died one year and eight months later. In my experience this is the only case of carcinoma of the cervix after sub-total hysterectomy.

CLASSIFICATION OF CARCINOMA OF CORPUS UTERI.

18 cases.

Type	Cases	Per cent.
I	Operable	6 33.3
II	Clinically inoperable	7 38.9
III	Technically inoperable	5 27.7

Total survival rate 66.6 per cent. in 18 cases.

Type	Cases	Per cent.	Survived Per cent.	Mortality Per cent.
I	6	33.3	83.4	16.6
II	7	38.8	85.8	14.2
III	5	27.7	20.0	80.0

Result to patients in each year group.

Type I.—6 cases.

Year Group	Alive	Dead
2-4	2	0
4-6	1	1
6-8	1	0
10 and over	1	0

Survival rate = 83.4 per cent.

Type II.—7 cases.

Year group	Alive	Dead
0-2	0	1
2-4	3	0
4-6	1	0
10 and over	2	0

Survival rate = 85.8 per cent.

Type III.—5 cases.

Year group	Alive	Dead
0-2	0	3
2-4	0	1
6-8	1	0

Survival rate = 20 per cent.

The patients in this group were older women; seven were single, five nulliparous. Some of these cases were selected for radium and not hysterectomy owing to general adverse conditions of health. The operable rate, however, was found to be only 33.3%, when considering the extent of the growth. I now treat most cases of carcinoma of the corpus with radium and the results are satisfactory.

These cases of carcinoma of the uterus show the much more frequent occurrence of carcinoma of the cervix and especially of its occurrence in women who have borne children. The importance of post-natal care cannot be too highly stressed, as the neglect of lacerations and septic discharges may lead to precancerous changes in the cervix. Every woman should be carefully examined at the end of the puerperium and one or two months later, and treatment provided, when necessary, for any pelvic

abnormality. Post-natal care is a necessary part of the prevention of carcinoma propaganda.

The contra-indications for the application of radium are extreme anæmia and pelvic sepsis. Preliminary treatment should be carried out in these cases. In advanced cases radium is contra-indicated.

The method of preparation of the patient and the complications which may occur in radium administration are fully published in the *Marie Curie Hospital Report 1929*.

The patient must be kept in bed for about a week after radium application, owing to the risk of reactionary hæmorrhage in the first day or two. This is of rare occurrence. Sepsis may occur if drainage is not satisfactory and pyometra may develop. The cervical canal may become blocked by necrotic tissue. Dilatation and drainage should be carried out, as should antiseptic douching with acriflavine 1:1,000, or 1:2,000, saline solution. Subsequent doses of radium should not be given until the sepsis has completely subsided. Pelvic pain is treated with sedatives, rectal tenesmus and pain with suppositories, and rectal ulceration with olive-oil enemata.

There is no doubt that in advanced cases radium prolongs life and lessens suffering. In early cases the results are as favourable as those of surgery. There is practically no immediate mortality and it is hoped in time that, if the fear of treatment can be dispelled, patients will seek earlier advice. Further improvement in radium results will be obtained by the subsequent treatment by X-rays; the installation at the Marie Curie Hospital is of such recent date that I cannot form any personal opinion as yet of its value.

(2) IN UTERINE HÆMORRHAGE (NON-MALIGNANT). TOTAL CASES, 85

All the patients had a preliminary curettage and biopsy. The majority have been kept under observation for two or three years or longer. It is most important that women suffering from uterine hæmorrhage should have a curettage and microscopical examination of the endometrium in order to exclude the presence of carcinoma. Hæmorrhage after intercourse in older women is an early sign of carcinoma of the cervix in some cases, and in old women a watery discharge may indicate carcinoma of the corpus. If a pelvic examination is refused the medical attendant should not take any further responsibility.

Radium in the treatment of uterine hæmorrhage has several advantages over hysterectomy. It involves little risk and the treatment takes a short time; this is a consideration for women earning their living. There is no mutilation by removal of the uterus, which sometimes causes a subsequent neurosis, owing to the patient's fears of being desexed. In hospital practice radium therapy is a cheaper form of treatment than that by drugs or endocrine therapy.

When given with care, radium should not interfere with menstruation except in cases of women at or near the menopause. Radium is most valuable in cases of menopausal hæmorrhages. In one case which I treated with radium for intractable hæmorrhage (in a young woman) normal pregnancy occurred some years later followed by successful childbirth.

UTERINE HÆMORRHAGE.

85 cases.

(A) Menorrhagia of puberty. 4 cases.

Average age 16 years 3 months.

Doses 200-600 M.E.H.

Duration of time since treatment:—

1 case treated two years ago.

2 cases treated six years ago.

1 case treated seven years ago.

Result: Cured, all had return of normal menstruation

(B) Uterine Hæmorrhage (non-malignant). 52 cases.

Average age 43 years 8 months.

44 cases (84.6 per cent.) marked improvement.

1 case (1.9 per cent.) slight improvement.

7 cases (13.5 per cent.) no improvement.

Of these last 7 cases:—

- 5 did not return.
- 1 had "second dose", lost sight of.
- 1 suspension of uterus; hæmorrhage ceased.

10 patients had normal periods after treatment.

Doses 200-600 M.E.H.

(C) *Menorrhagia due to fibroids.* 29 cases.

Operation refused or inadvisable.

Average age 46 years 5 months.

Doses 412-5-2200 M.E.H.

24 cases (82.7 per cent.) marked improvement.

1 case (3.4 per cent.) lost sight of.

4 cases (13.8 per cent.) no improvement.

Of these last 4 cases:—

3 had subsequent hysterectomy.

1 died four days later, of pulmonary embolus; pelvic sepsis was present.

Menorrhagia of puberty is, fortunately, of infrequent occurrence. It is very difficult, in some cases, to treat it successfully. In the four cases treated with radium in this series, all previous methods of treatment had failed. These included drugs, endocrine extracts, and, in one case, electrical therapy. All these cases were cured and menstruation became normal. In one case the dose had to be repeated. The determination of the dose requires great care and the smallest amount possible is given in order not to interfere with the reproductive function.

The majority of the cases of menorrhagia in Group B were in older women. If radium is applied about the time of the menopause the periods, as a rule, cease. Sometimes it is necessary to give subsequent endocrine treatment for menopausal symptoms but as a rule these are not so prolonged as after the normal menopause. Anæmia, when present, must always be treated with iron and tonics. If anæmia is severe it is necessary to raise the hæmoglobin index before applying radium. Rest in bed, dieting and tonics are advised beforehand for several weeks. In severe cases a preliminary blood transfusion may be necessary.

I do not advocate radium therapy in the case of fibroids as an alternative to surgery; I think that surgery gives better results. These cases of hæmorrhage due to small fibroids or to chronic pelvic adhesions were unsuitable for operation, or the patients were unwilling to give up the time or take the risk of an operation. In cases of fibroid there is the risk of blocking of the cervical canal and it is necessary to make sure that there is ample drainage by sufficient dilatation before the radium is applied, otherwise a pyometra may develop. The treatment in such a case is dilatation with intra-uterine antiseptic douching. Obviously radium therapy is contra-indicated in cases of sterility.

I have found in a number of cases that one or two periods after the application of radium have been profuse, owing to a certain degree of radium reaction. This, however, is only temporary but it is as well to warn the patient that it might occur.

A number of the patients were treated in the Marie Curie Hospital. I am also much indebted to Mr. Hill, the Radium Officer of the Royal Free Hospital, for helping me with the follow-up of the patients treated there.

Discussion.—PROFESSOR FLETCHER SHAW said that of late years there had been great improvement in the treatment of carcinoma of the cervix. He was old enough to remember the time when early cases were treated by vaginal hysterectomy and the patients had had on the average, a shorter life than those in the advanced cases which were treated only by cauterization. Wertheim's hysterectomy was the first great advance and he had had the privilege of assisting his old chief, Professor Donald, when he performed the first two in Manchester and of doing the third one himself. Mr. Victor Bonney was the great exponent of this operation in this country and his latest figures for 384 cases showed 39% alive and well after five years and 20% after ten years. His (the speaker's) own series over five years were 154 and of these 38.4% were alive and well; 27% of these after ten years. These figures were so close to Mr. Bonney's that they might be taken as the standard of what could be achieved

by this operation. Radium was the next advance and if it gave as good results as surgery did it was preferable, as the patient was saved the discomfort which many had in the convalescent period after such a severe operation. Ten years ago foreign statistics were numerous, but there were none from this country, although the radium centres in London and Manchester had been working on these cases for many years and, he was sorry to say, these centres were still silent. As it was impossible to abandon such a successful operation upon foreign statistics alone, without any knowledge of what the English radiologists could do, Professor Dougal and himself decided to purchase their own radium and experiment upon their own cases and, after much investigation—in which they were helped by the staff of the newly formed Marie Curie Hospital—they decided to follow the technique of Heymann in Stockholm. The results could only prove whether this method was satisfactory or not, but it was felt that this would be more useful than a series of small numbers done by different methods. Professor Dougal and himself now had 94 cases treated more than five years ago and of these 39—that is 41.3%—were alive and well, which was a better result than he had had from Wertheim's operation alone. But the results of radium were even better than this figure as every case could be treated by radium while the operation could only be performed upon the less advanced cases. It was notoriously difficult to classify cases of carcinoma of the cervix into the four stages, but of these 94 cases they had classed 38 into stages 1 or 2—that was to say, as being operable—and of these 19 (50%) were alive and well at the end of five years. They felt, therefore, that there was no doubt that in their hands radium was giving better results than Wertheim's operation, which they had now abandoned. Although these figures showed a great advance in the treatment of carcinoma of the cervix, no one could feel perfectly satisfied with a 40% freedom from recurrence after five years.

Dr. LOUISA MARTINDALE said she had not found that carcinoma of the fundus occurred much less frequently than carcinoma of the cervix. In her own series of 207 cases of carcinoma of the uterus, 81 cases were of fundus, and 126 of cervix, carcinoma, the former occurring more often in private practice, whereas nearly all the cervix cases were in hospital patients. Of the 81 fundus cases, she had operated on 42, and used radium, or radium and X-rays on 31, and deep X-rays for recurrence in the eight other cases.

In 60.6% of the operated cases, and in 57.8% of the cases treated with irradiation, the patients were alive and symptom-free over five years, but the operated cases included the earliest and the most advanced cases, for in two of the latter she had had to perform extensive intestinal resections, as the growth had already invaded the gut.

Mr. T. F. TODD said that the co-operation of the physicist, in particular, was required to control the dosage problems. The whole subject was confused by the use of the term "milligramme-hours", which was merely a time-quantity statement and gave no indication of the amount of radiation delivered to the tumour. It was necessary to consider other factors, such as filtration, type of applicator, and distance of radium from the tumour. Slipshod terminology like this only served to bring discredit upon gynaecologists. The question of constitutional reaction to radiation was most important. If routine blood-counts were taken twice weekly during the whole course of treatment it would be found that total lymphocyte counts were steadily falling, and towards the end might be as low as 200 or 300. Such a patient was really ill, and would be an easy prey to any infection. Such routine lymphocyte counts were found useful in practice, enabling one to avoid excessive treatment in particular cases. Dame McIlroy's suggestion that cervical erosions might be treated by radium was, he thought, unsound. He did not know how much or how little radium could be used in the vagina or uterus without causing ovarian damage, possibly irremediable. The same criticism applied to the treatment of puberty menorrhagias; there was no scientific basis for a selective control of these cases.

DAME LOUISE MCILROY (in reply) said that in some cases of menorrhagia of puberty, previous treatment had failed and radium should only be applied in these cases of failure. Antuitrin was an expensive form of treatment for hospital cases but was successful in most cases in private practice. In cases of carcinoma of the corpus the incidence in hospital practice was small compared with that of carcinoma of the cervix. Erosions of the cervix were found to have disappeared in some cases after intra-uterine radium treatment for hæmorrhage. Cystoscopy was carried out in all cases in which bladder involvement was suspected. The third type of carcinoma of the corpus was that of a very advanced condition of the disease. The fibroids were small as a rule and in some cases multiple. The polypoid type of submucous fibroid was better treated by removal.

The Prolapse Syndrome

By A. C. PALMER, F.R.C.S.

THE term "prolapse syndrome" means prolapse associated with excessive bleeding from the cavity of the uterus. When, on straining, the cervix protrudes for an inch or more from the vulva, the form of the prolapse becomes typical of that denoted by the term.

In the early part of this century removal of the uterus by the vaginal route was largely abandoned in favour of the abdominal route, by those gynaecologists with whom I worked. This change was partly due to the fact that gynaecologists were becoming surgeons rather than physicians, and partly because in a large number of cases abdominal hysterectomy is obviously the method of choice.

From 1919 onwards it became my portion to operate on a number of 14-stone patients possessed of an enlarged uterus, the "adipose sporran", and varying degrees of prolapse, and complaining of excessive bleeding, accompanied by such general impairment of physical capacity as merited hysterectomy for its cure. These cases were dealt with by the abdominal route, the three or more inches of subcutaneous fat and the "sporran" making the opening and closing of the abdominal wall in itself an operation of some difficulty.

Being then free from bleeding, the patients, in the course of time, regained some of their former energy and physical enterprise, and began to notice their disability from prolapse. They required anterior colporrhaphy and posterior colpoperineorrhaphy, and in the case of some, whose former operation had been a sub-total hysterectomy, a hypertrophied actively-discharging cervix required removal as well. A few required belts or further operation for incisional herniae.

A Combined Operation

In thinking about this matter the question naturally arises: "Why not carry out a vaginal hysterectomy and combine it with the reconstruction operation?"

I began tentatively to combine the two operations, and up to the present time have found the procedure satisfactory to the patient and surgeon in suitably selected cases—namely, those whose symptoms and physical signs are denoted by the term "prolapse syndrome". This term, while including the prolapse sign and symptom complex, is meant to have a wider application, and extend to those patients who have an enlarged or retroverted uterus, or both, and complain of excessive bleeding, the condition of the uterus being such as to render practicable its removal from below.

Common Prolapse Symptoms

(1) Girdle-ache, including sacral backache and dragging pain in the inguinal regions.

(2) A sense of discomfort from something coming down in the perineal region.

(3) Frequency of micturition, varying in degree up to stress-incontinence.

(4) Irritation from excessive cervical discharge.

(5) Undue fatigue at the end of a routine day.

Conditions Necessary for Easy Performance of Vaginal Operation

(1) The uterus and appendages must be mobile.

(2) The uterus must not be too large or associated with large tubal or ovarian swellings.

(3) The uterine disease must be such as not to contra-indicate its removal from below—that is, carcinoma of the cervix.

(4) The cervix should come down readily to the vulva.

(5) The vaginal outlet should be relaxed, or at least easily enlarged by a relatively small incision, something considerably short of the old Schuchardt's incision.

Quite often these patients have the fat, more or less pendulous, abdomen, unsuitable for abdominal incision.

Technique of the Operation

Five operative procedures are combined, (1) anterior colporrhaphy, (2) vaginal hysterectomy, (3) reconstruction of the hernia of the pouch of Douglas, (4) posterior colporrhaphy, (5) perineorrhaphy.

I will briefly describe a standard method of linking these procedures.

(1) Preparation of the field: The perineum is incised back to the anal margin. The nymphæ are sutured to the thighs and traction sutures are inserted in the cervix. The area of vaginal mucosa to be removed is determined: (a) of the anterior mucosa, a landmark suture being inserted to mark the upper end of the new anterior vaginal wall, and (b) of the posterior vaginal mucosa, landmark sutures being inserted at the site of the upper end of the new posterior vaginal wall.

(2) Removal of redundant tissue: The anterior and posterior mucosa and the uterus are removed in one technique.

(3) Reconstruction of the pelvic diaphragm: The uterine stumps and ovario-pelvic stumps on either side are fixed to the upper margin of the new lateral vaginal walls. The cut edge of the peritoneum of the utero-vesical pouch is joined to the anterior landmark sutures, thus forming the upper end of the new anterior vaginal wall.

(4) Reconstruction of the anterior vaginal wall.

(5) Removal of redundant peritoneum of the hernia of the pouch of Douglas: The peritoneal stumps are sutured to the posterior landmark sutures, thus forming the upper end of the new posterior vaginal wall.

(6) Reconstruction of the posterior vaginal mucosa and the perineal body.

The operation in my hands requires from an hour to an hour-and-a-quarter for its performance, without undue difficulty in the control of unexpected oozing. There is, as a rule, no appreciable shock, and the patients do not have a stormy post-operative period. Towards the end of a week there is usually some vaginal discharge, which clears up readily with douching. The length of stay in hospital and the after-convalescence period is the same as that for simple repair operations.

Advantages of the Method

- (1) The avoidance of two operations and the prolonged period of convalescence associated therewith. Approximately five weeks instead of ten.
- (2) The avoidance of an abdominal incision in fat women and the possible post-operative complications.
- (3) The relative absence of post-operative shock.

I have looked up the notes of 116 cases. In all, the anatomical result at the time of departure from hospital was good and the patients' general condition satisfactory.

Ninety-eight patients have been examined twelve months or more after operation, and nine, three months or more. The anatomical result was good in all but two cases. In one case the posterior fornix, owing to imperfect fixation, bulged down to the outlet, on straining, as a hernial protrusion. This gave rise to some discomfort, and has been repaired with success. In one recent case that, of a very fat patient, the condition of the anterior vaginal wall is only fair, three months after operation; it comes down almost to the vulva on straining and this result is below standard. Eighteen out of the 116 cases had post-operative *B. coli* cystitis, but in eight of these it was known to be long-standing. In sixteen of these cases it occurred in the first sixty cases before the introduction of a self-retaining catheter and daily bladder-wash was adopted as a routine. There were five slight secondary hæmorrhages, one on the seventh day, and four between the tenth and twelfth days. Two patients had small abscesses in the perineum, which cleared up.

One case proved fatal. This happened in a mentally deficient woman who, by means of her fingers, removed the perineal stitches, became septic, and ultimately died from a pulmonary embolism. It is unfortunate that we were unable to recognize the woman's mental condition previous to the operation, for failure to do so has impaired what might otherwise have been an unblemished record.

Section of Odontology

President—W. WARWICK JAMES, O.B.E., F.R.C.S., L.D.S.E.

[April 26, 1937]

A Comparative Study of the Innervation of the Periodontal Membrane

By W. LEWINSKY and D. STEWART

(From the Anatomy Department, The Victoria University, Manchester)

INTRODUCTION

THE first description which we have been able to trace of nerves in the periodontal membrane was given in 1837 by Linderer. He stated that this membrane was amply supplied by nerves and blood-vessels, which appeared in great numbers, often parallel, connected with each other and passing from the base of the alveolus towards the gingival margin. Czermak (1850) demonstrated nerve-fibres in the periodontium by clearing the section with acetic acid. Wedl (1870) described nerve-fibres of different diameter, originating from the dental and gingival nerves. He was the first to suggest that they also enter the membrane from spaces in the alveolar wall. Boedeker (1883) states that he has met with but few fibres in his specimens of the membrane. Black (1887) has given a fairly comprehensive study on the nerve supply of the membrane. He describes the principal bundles entering by way of the apical space and a considerable number of nerve-bundles which enter through the wall of the alveolus, each containing from 4 to 10 fibres. He states that specialized nerve terminations have not been found in this membrane in sufficient numbers to show that they are essential. He has seen a few Pacinian corpuscles near the gingival border and occasionally some other knob-like terminations. Generally, however, none of these is found. He suggests that the nerve-fibres divide into single filaments and probably terminate mainly as naked fibres. Retzius (1894) found periodontal nerves in amphibians. Huber (1899) states that there are undoubtedly nerve-fibres in this membrane. Hopewell-Smith (1919) reports that the exact manner of the distribution and nature of the ultimate terminations and ramifications or anastomoses of the nerve supply of the root membrane is unknown. It is a branch of dental histology which has been practically ignored. Mummery also, in 1912, had to say that he had seen very numerous nerve-fibres in the periodontal membrane in specimens impregnated with silver-nitrate, but it was very difficult to procure sections in which they could be traced for any distance. Dependorf (1913) gives a detailed account of the innervation of the periodontal membrane. He describes three different groups of nerve-fibres:—

- (1) Parallel thick longitudinal nerve-fibres or bundles.
- (2) From these, thinner nerve-bundles branch off at an acute angle.
- (3) Single myelinated and unmyelinated fibres branch off the two previous types.

The nerve-bundles form coarse and fine networks and end in fine pointed processes, particularly in the cementoblast region. In more recent times Sicher (1928), mentions that the manner of termination of nerves in the membrane is unknown, while Kadanoff in the same year was able to produce an interesting study on the membrane. He disagreed with Dependorf's conclusions as to the nature of the endings of the nerve and considered that as the latter had used extracted teeth, the material might have been damaged. He himself was fortunate enough, by using material from two

individuals who had suffered death from judicial hanging, to obtain the alveolus and tooth in one piece which he stained by the Bielschowsky method. He found nerve-fibres from the apical region running vertically towards the gingival margin and being joined by bundles entering the membrane through the foramina in the alveolar processes. The smaller nerve-fibres appeared to end in terminal plexuses but there was no anastomosis. Some of the terminal fibres ended in small knob-like swellings, but there were no encapsulated nerve-endings. He differs from Dependorf who stated that a part of the nerve-fibres end in the cementoblast region and asserts that those fibres which enter form loops there and then return to the connective tissue of the membrane. He denies the existence of any innervation of the cementoblasts and therefore of the cement. Ochoterena (1933) described the nerve-endings in the periodontal membrane as free terminations or fine varicosities which go round the organ ending at different levels.

Van der Sprenkel (1934-6) recently published a series of papers on this subject. He used the mandibles of young mice stained by the Castro-somnifen method, and according to him, the nerve-fibres in this membrane end in three ways:—

- (1) End-rings with a periterminal network situated near the alveolar wall.
- (2) Terminal networks near connective tissue nuclei.
- (3) A nervous network from which nerve-fibres passing through the cementoblast region go over into the dentine to end with very delicate rings inside the dentinal tubuli.

He suggests that the intradentinal nerve-fibres form a connexion with those periodontal fibres and their exceedingly minute rings within the dentinal tubuli.

Bradlaw (1936) has been unable to find the terminal rings of van der Sprenkel but he describes the neural loops of Kadanoff turning back from the cementum and also structures which appear to be terminal coils near the cementum.

It is to be noticed that except for Bradlaw, none of these investigators illustrate their work with photomicrographs or employ serial sections in their researches. However, Dr. van der Sprenkel has very kindly sent to us some copies of his unpublished photomicrographs which we have found of great value in comparing his results with our own.

METHOD

Encouraged by the results which we obtained in studying the innervation of the dentine, where we had been able to trace the whole course of nerve-fibres of the pulp for a considerable distance in passing through the odontoblasts into the dentine, we decided to employ the same staining method, namely the Cajal silver-nitrate impregnation method, for the study of the innervation of the periodontal membrane. For the human periodontal membrane we used extracted teeth which had portions of the alveolus attached. For the animal investigations, the jaws of freshly killed animals were removed and divided with a fret-saw so that we obtained smaller pieces of the jaw containing one or more teeth. The material was fixed in ammonia alcohol and then decalcified in 5% nitric acid. After washing in running and distilled water, the pieces were impregnated by the ordinary Cajal technique. They were then embedded in paraffin and cut in serial sections at 12μ thickness, both in the longitudinal and in the transverse plane. We have cut thicker sections, but we found either that they curled up and could not be mounted efficiently, or that the clearness of the finer fibres could not be brought out satisfactorily. By this method, we succeeded in following the course of the nerve-fibres for a considerable distance, tracing them from section to section. By means of the camera lucida, a drawing of one section was made which showed the edge of the tooth and the alveolus. Then all the nerve-fibres or parts of them in this particular field of the periodontal membrane were sketched in their correct orientation. The next section was then adjusted under the microscope so that the images of the principal landmarks fell on the corresponding positions of the drawing of the first section and the fibres or

portions of fibres not seen in the first section were now added to the drawing. This procedure was followed in further sections as required, and in this manner a linear reconstruction was reproduced which showed the course of the nerve-fibre through two or more sections.

We began our study by using human teeth with the alveolar plate attached, and obtained results which corresponded in many ways with those of Kadanoff, who used human material also. These results were not unlike those of Bradlaw, who studied the periodontal membrane of the monkey, but they were entirely different from the findings of van der Sprenkel, who obtained his material from the jaws of young mice. We have suggested, in our two recent papers on this subject, that these marked discrepancies may be explained by the different material. We therefore extended our studies and examined specimens of readily obtainable mammalian genera.

PERSONAL OBSERVATIONS

The nerve-fibres for the supply of the periodontal membrane arise from the main trunk of the dental nerve and then pass towards the apex of the tooth. Here the fibres which go to the pulp of the tooth pass into the apical canal and do not concern us any further in this communication. The nerve-fibres for the periodontal membrane run to supply that tissue, either by passing upwards from the apex of the tooth through the membrane itself or they come off nearer to the main nerve-bundle and run peri-



FIG. 1.

KEY TO LETTERING ON FIGURES

B = bone; C = cement; N = nerve; Ne = nerve-ending;
Nt = nerve-trunk or bundle.

pherally in the alveolar processes themselves and pass into the periodontal membrane by perforating the alveolar processes at different levels. This description is the one generally accepted and up to this point we agree with it. The fibres which enter from the alveolar plate are then said to turn peripherally towards the gingival margin. We have, however, been able to show (fig. 1) that this is not a complete description of what actually occurs. This photograph, which was taken from a tooth in situ in the ferret, shows the nerve-bundles entering the periodontal membrane from the

alveolar plate, which forms a black band in the figure. It will be seen that the fibres do not all turn peripherally towards the gingival margin but divide into two bundles of approximately equal size, one bundle of which turns peripherally, but the other turns centrally towards the apex. We have been able to observe this in several different types of mammals and we have already published (Lewinsky and Stewart, 1937) a photomicrograph illustrating a similar subdivision of the nerve in the cat. The actual canal by which the bundle enters the membrane through the bone cannot be seen in this specimen (fig. 1), but it is clearly present in the previous section. We have also been able to observe this arrangement of the nerve-fibres in the human.

The nerves of the periodontal membrane, whether they come from the apex or whether they enter from the alveolar plate, in the first place run longitudinally and



FIG. 2.

more or less accompany the course of the blood-vessels. Ultimately, of course, the nerve-fibres must end, and it is particularly this part of the problem that we desire to discuss in this paper. It will be found that there are essentially two different types of nerve-endings, one a free arborization with very fine terminal fibres, the other a definite end-organ. As there are distinct differences in the distribution and the manner of ending of the nerves in the different orders of mammals, it will probably be more satisfactory if we deal in the first place with these individually and then discuss the general bearing of our results.

Carnivora

Cat.—In this animal, we found two different types of nerve-fibres, coarse and fine. The coarse fibres were distinctly thicker but were less heavily impregnated. They

had a dark brown appearance, whereas the finer fibres were frequently stained intensely black. The coarse fibres always ran in the outer part of the membrane, whereas the finer fibres bent inwards and ended in fine ramifications more centrally, and very often near the cementum. Although the impregnation in several of our specimens was very satisfactory, and even the finest fibres were clearly demonstrated, in no case were we able to find any of these fibres entering the cementum. The coarser fibres, on the other hand, terminated in special end-organs which were spindle-like in shape and were formed by the nerve-fibres becoming twisted like a spiral spring (fig. 2). At intervals on the convolutions there were rounded thickenings. This end-organ in the cat has no special relationship to any particular cells, neither does it form a network, but has a spiral-like course without any side branches or reticular



FIG. 3.

endings. Occasionally a rather different type of ending was observed, bearing a close resemblance to the organs of Ruffini, and an example of this is given in fig. 3. Though at first sight these nerve-endings appear to be different in structure, a study of a number of them reveals that they consist of a single nerve-fibre, more or less convoluted and twisted upon itself, and they are all situated in the outer part of the membrane. In fig. 4 an example is given of the other type of termination in fine arborizations. It also illustrates the method of reconstruction which was described earlier in this paper. Fig. 4c is the actual reconstruction from four consecutive sections, and photomicrographs of the first and last sections of this series are presented in 4a and 4b. At the periphery of the membrane a bundle of coarse fibres will be observed, with a coiled end-organ. The finer fibres are placed more centrally and it will be observed that they terminate in arborizations which do not run to the cementoblasts.

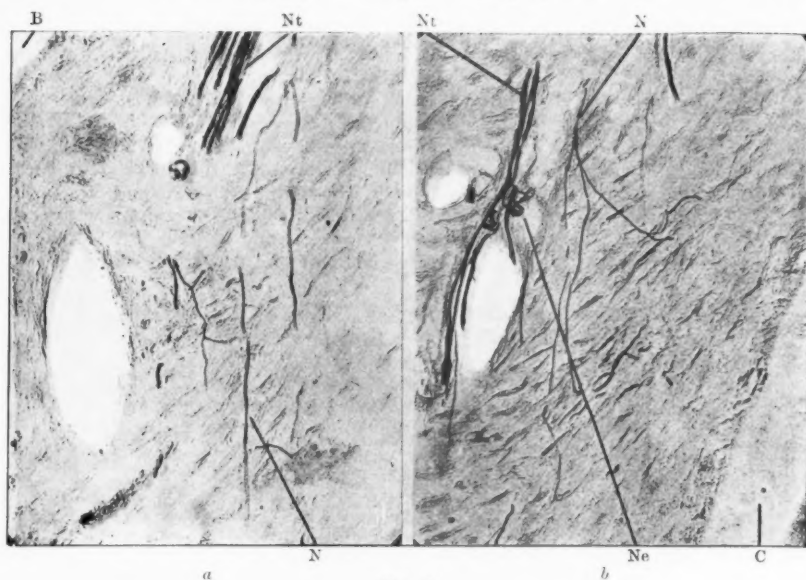


FIG. 4.



FIG. 4c.

Ferret.—We have also examined the periodontal membrane in this animal as a further example of the carnivora. We found the same coarse type of fibres with coiled specialized end-organs but the latter are smaller and less complicated. The finer fibres with terminal arborizations were also present.

Rodents

In the rodent the texture of the bone is much less dense than in the carnivore and has larger marrow spaces in which the nerve-fibres run. This is particularly noticeable in the incisor tooth where the main nerve-bundles run in relationship with the tooth for a considerable distance. These give off fibres which have a similar course to those already described in this paper.

Rabbit.—After the fibres enter the periodontal membrane they have a similar distribution to that which has already been described in the carnivora, namely they either end as very fine fibres or as definite end-organs. These end-organs, however, are of a different type from those which we have illustrated in the cat. Fig. 5 illustrates both types of nerve-ending as seen in the rabbit. Towards the outer side of the membrane lying next to the alveolar bone, there is a coarse branching nerve-ending containing many irregular knob-like swellings, the whole having a spider-like appear-

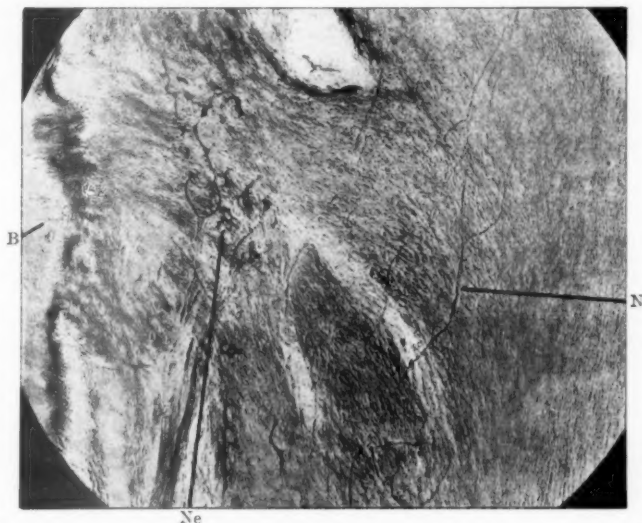


FIG. 5.

ance very different from the spiral-like ending of the similar thick fibres in the carnivore. Lying more medially near the cementum, thinner fibres will be observed, which resemble the finer fibres in the cat. One or two dichotomic divisions will be observed. Many of these end-organs have been observed and they all have a coarse branching form, sometimes with an irregular swelling, but their shape and size vary considerably from end-organ to end-organ.

Mouse.—In the mouse we find the same general arrangement as in the rabbit, and the nerve-endings are of the same spider-like form. Fig. 6 is a medium-power magnification of the periodontal membrane in the mouse. This gives a general view of a portion of the membrane and shows very clearly the frequency with which the "spider-like" ending can occur in certain parts of that tissue. Fig. 7 shows another spider-like ending under a higher power. It will be observed that it lies to the outer side of the periodontal membrane and is separated from the main nerve-bundle by a thin layer of bone. This section was taken from an incisor tooth. The finer fibres are similar in appearance to those already described in the cat and the rabbit, and end

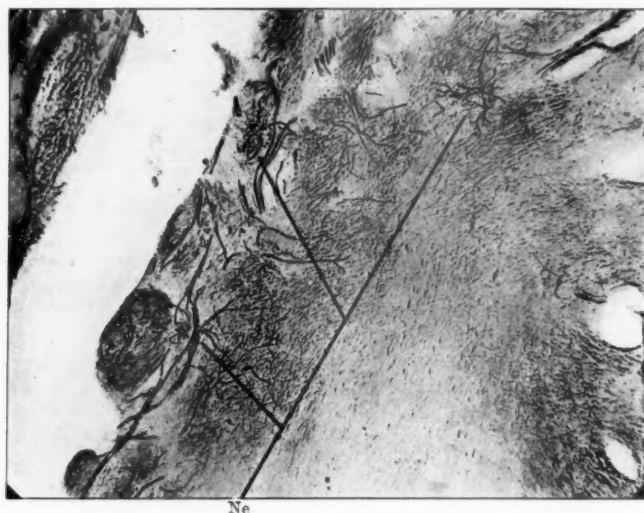


FIG. 6.

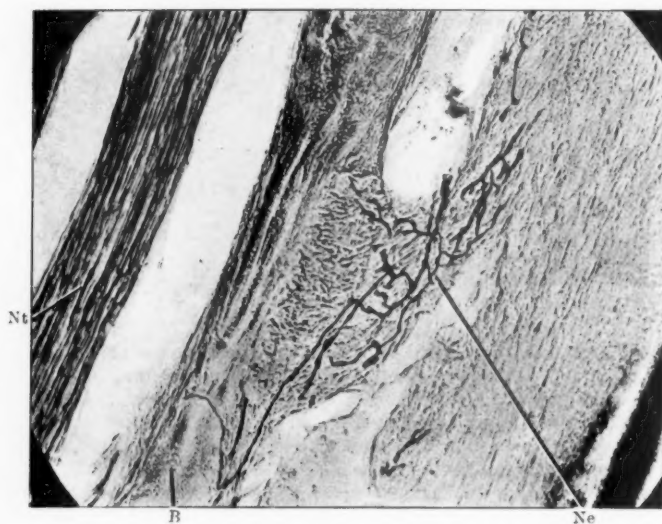


FIG. 7.

in arborizations in the inner region of the membrane. We have also observed fibres giving a loop-like arrangement similar to that which has been described by Kadanoff in the human but not placed as close to the cementum as he described. It is reminiscent of the loop-like arrangement mentioned by Bradlaw.

Insectivora

The examples of the insectivora which we have been able to investigate have been the mole and the hedgehog. In these we have been able to observe little in the nature of a specialized end-organ. It is possible that this may be due to faults in technique, but we think this is unlikely on account of the depth to which the fibres have been stained. The general distribution of the fibres in the hedgehog



FIG. 8.

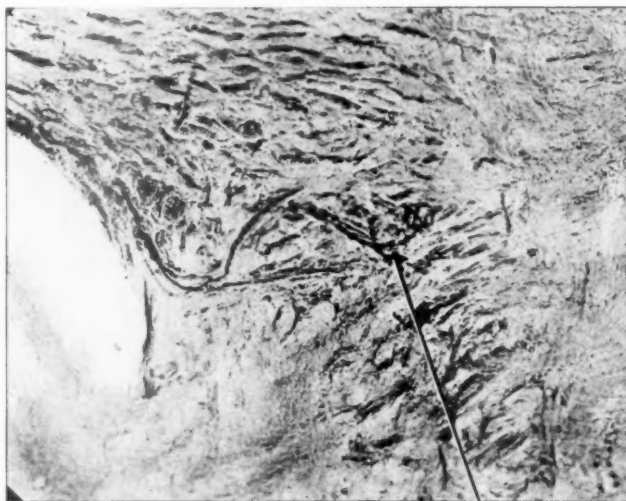


FIG. 9.

is shown in a reconstruction of two sections in fig. 8. Here the fibres are seen dividing and forming arborizations but no encapsulated end-organs will be observed. When we come to discuss the human, it will be seen that the general distribution of the nerves in the insectivore more closely resembles that in the human than any other which we have yet described. In this order a further type of nerve-ending is found in the periodontal membrane; in fig. 9 several of the fibres terminate in a knob-like

swelling which, as we shall see later, is similar to what occurs in man. The arrangement of the nerve-fibres in the mole is very similar to the conditions found in the hedgehog. Fig. 10 shows the distribution of nerve-fibres in the periodontal membrane of this animal, and again it will be observed that the fibres form an arborization without definite end-organs. We have been fortunate, in this specimen, to be able to photograph a great length of the fibre and are thus able to show its distribution over a considerable distance.

Human

In the human, the nerve-fibres have the same general course and arrangement as that described at the beginning of this paper, with reference to the mammals generally. As they proceed towards the gingival margin, individual fibres leave the main bundles at intervals, and after a short course divide dichotomously into small branches. In the human there is not the same clear differentiation into the two types of fibres and endings which we have already described, but a careful examination of the specimens revealed that the two types are probably also present.



FIG. 10.

One type (fig. 11) appeared to consist of long thin fibres which split off finally into still finer fibres having a knob-like swelling at the end. These endings were observed mainly near the alveolar bone or in the middle of the membrane. The other type after dichotomous division ended in very fine arborizations. Sometimes in these arborizations, the knob-like endings mentioned in the preceding type of fibre were also observed. These are illustrated in figs. 12a and 12b, the former being a two-section reconstruction. We have published examples of the arborizations and the knob-like endings in a recent paper (Lewinsky and Stewart, 1936).

Some of the rounded endings appear to be in direct contact with the cells of the periodontal membrane but, as many have no relationship to these structures, it is doubtful whether this finding has any importance. These endings resemble the structures seen by Kadanoff, so that it is impossible to compare the two structures with certainty. In the introduction to this paper mention was made of the loop-like arrangement of the fibres as described by Kadanoff and also of a similar



FIG. 11.

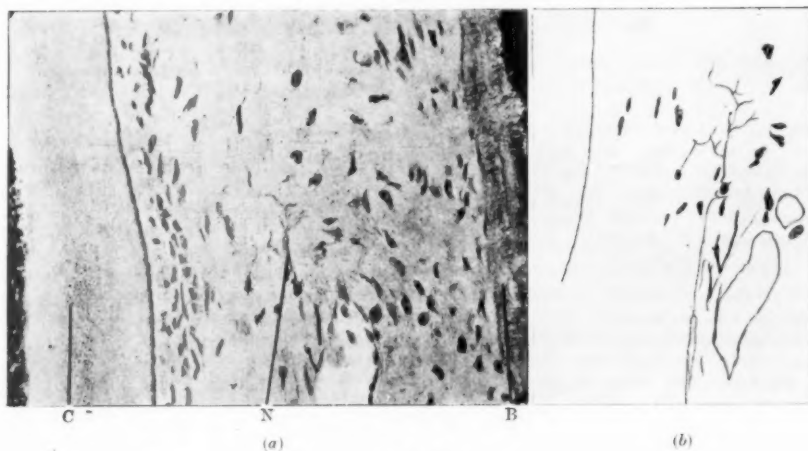


FIG. 12.

but rather more complicated form seen by Bradlaw in the monkey. In fig. 13 we are able to demonstrate this loop-like arrangement in the human. It resembles more closely the conditions seen both by Kadanoff and by Bradlaw. It will be noticed that this loop lies in the part of the membrane near the cement.

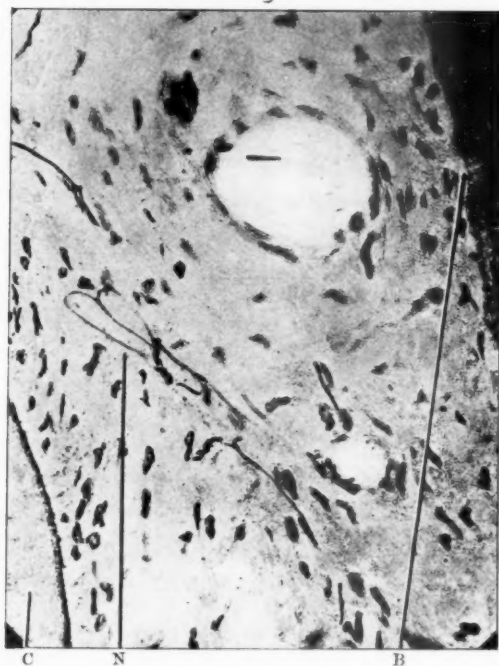


FIG. 13.

DISCUSSION

It is rather difficult to correlate our findings in the different classes of mammals into a definite theory, but we have at least established the existence of two different types of nerve-endings which are usually situated in different parts of the periodontal membrane. These are :—

(1) End-organs which always lie towards the peripheral part of the membrane and are associated with a thicker type of fibre. Although their appearance differs in different classes of mammals, there is a definite relationship between the individuals of each order in which these fibres have been seen. The carnivora, represented by the cat and the ferret, show a single thick fibre more or less convoluted and twisted upon itself and situated near the alveolar bone. The rodents, represented by rabbits and mice, exhibit a coarse-branching nerve-ending with a spider-like appearance, also situated in the outer part of the membrane. In the insectivora, however, we have only been able to find fibres which terminate with knob-like swellings. In the human we found a similar type which is also situated in the peripheral part of the membrane. This is also a single fibre running for some distance without branching and ending in one or more knob-like swellings. It is interesting to note that the insectivora are more closely related to the primates than any other mammalian order. Our results therefore suggest, but this will require confirmation by further work, that each of the mammalian orders may have its own characteristic Type 1 ending.

(2) The second type of fibre most probably represents a final ending as well, although these fibres never show any definite end-organ. They are very thin fibres which were seen in all

the different orders of mammals and were situated nearer the cementum than those in Type 1. Sometimes they form loops, very often they divide dichotomously and in the human, the cat and the insectivora end in very distinct arborizations.

The presence of these two types of nerves with their different distribution and terminations would suggest that they have different functions and therefore conduct to the central nervous system different types of sensory impressions. Ranson and Hess have described coarse, medium, and fine fibres in the roots of the spinal nerve. As a result of their animal experiments they produced evidence that the fine fibres most probably transmit painful stimuli while the coarse fibres conduct pressure and touch sensations. More recently, Woollard (1936) stressed a similar differentiation of function in his work on the nerve supply of the human skin. Windle (1927) too investigated this problem in regard to the pulps of the teeth and found that in the cat and dog the myelinated fibres were of the small or medium type and that no large fibres were present. He devitalized the teeth by removing the pulps, and discovered that most of the reacting cells in the Gasserian ganglion were also of the small or medium type. These cells are considered to be the cells for the finer or the medium fibres, and hence are connected with the transmission of painful stimuli. Brashear, who repeated the work done by Windle, included in his investigation the fibres of the periodontal membrane of the cat. His results regarding the pulps were very similar to those which Windle had obtained. Furthermore, Brashear (1936) found that fibres of all sizes were present in the peridental tissue of the cat. About 20% of the fibres in this tissue were of the large type— 10μ or larger in diameter. After the teeth had been devitalized he found, from the reaction of the cells of the Gasserian ganglion, that the nerve-fibres of the pulp have nothing to do with pressure and pressure must be transmitted along the thick nerve-fibres of the peridental tissue, as in the pulp there were only small and medium-sized fibres. This confirms the observations of Stewart (1927) that the tooth was still able to localize small degrees of pressure after the pulps had been removed. Brashear further states that

"The sense of pain is not easily aroused in the peridental tissue, but when aroused, this tissue is as painful as the average of tissues, as is shown in acute peri-cementitis."

In the rodents and carnivora we can confirm quite distinctly these two different types, namely the thick and thin fibres, and we feel that the explanation of their responsibility for pressure and pain is very strongly suggested by our observations. In the human, however, although we have found two different types of nerve-endings, the difference in diameter in these two types is not so great.

Like Kadanoff and Bradlaw, in spite of a most careful examination of all our specimens we have never been able to discover any nerve-fibres which were penetrating the cement, much less entering the dentine. In transverse section, however, it has been our experience that the Sharpey's fibres are more distinct, and it might be possible that in preparations in which the ground substance was over-impregnated, these Sharpey's fibres or portions of them might give the appearance of nerve-fibres. We have found the recurrent loops which Kadanoff and Bradlaw mention. These are made by nerve-fibres turning back on their course after approaching the cement. We have also found these loops, however, inside the periodontal membrane proper and in our specimens they have not entered, as far as we could observe, the cemento-blast layer. The terminal coils which Bradlaw demonstrated clearly, with his photomicrographs, in the monkey, have not been found in our specimens. We had, however, considerable difficulty in obtaining monkeys' jaws, and those which we got were unsatisfactory, partly owing to the inferior quality of the staining and partly to post-mortem changes which had taken place in the nerve-fibres before they came into our possession.

It will have been clear from our description of the nerve-endings observed in the rodents, that they are quite different from the structures described by van der Sprenkel. The only thing which they have in common is that they tend to lie in the outer part of the periodontal membrane. Structurally, van der Sprenkel's end-organs are of two types, namely, end-rings with a peri-terminal network, and networks around connective tissue nuclei. The end-organs which we have seen have ended in coarse branches with a spider-like appearance, which certainly do not anastomose with each other and do not form a network. The question which now requires an answer is how to explain the differences in the results. We suggest that this may possibly be due to the fact that van der Sprenkel used embryonic material in which the teeth were at the earliest stages of their formation; he states that the cementum had not yet formed, and that only a small portion of the dentine was developed. He states that in fully developed teeth he has never been able to find nerve-endings:—

"In den weiterentwickelten zementhaltigen Zähnen, wo das Periodontium schon ganz aus kollagenen Bündeln besteht, habe ich nach Endigungen gesucht, auch näher dem Zahn auf den Strängen gelegen, aber ich habe keine gefunden."

There is therefore a possibility that the end-rings described by van der Sprenkel are embryonic endings in the development of the mature spider-like endings described by ourselves. On the other hand, van der Sprenkel appears to have relied mainly upon transverse sections, while the greater part of our investigation has been based upon serial longitudinal sections. We have, however, examined some transverse sections and have there seen structures which bear some resemblance to van der Sprenkel's end-rings. It will be observed, however, that they contain no network and we have some doubt as to whether they are the actual endings or not. Van der Sprenkel also describes a terminal network, presumably in the inner part of the periodontal membrane, from which nerve-fibres pass through the cement into the dentine and end there with very delicate end-rings. He suggests that these fibres connect up with the nerve-fibres which run from the pulp into the dentine. We have been unable, either in our mouse specimens or in any other animals, to find this terminal plexus, or to trace any fibres into the cement. The only other investigator who claims to have seen nerve-fibres ending in the cementoblasts is Dependorf, but even he was unable to trace them into the cement. However, none of the investigators except ourselves and van der Sprenkel has used rodent material. It is possible, therefore, that we have missed these structures altogether, but even so, we do not think that van der Sprenkel is justified in applying to the adult human the results which he obtained in the embryonic tissues of a mouse, especially as the consensus of opinion of those who have worked on human material is against this hypothesis. Until further evidence is available, we do not think it can be accepted that in man nerve-fibres enter the dentine from the periodontal membrane and anastomose there with fibres which have their origin in the pulp.

Stewart was able to show, in 1927, that the tooth had considerable powers of localizing small degrees of pressure and that this was still present after the pulps had been removed. He therefore suggested that the ability to localize pressure was probably situated in the periodontal membrane. Van der Sprenkel has enunciated the hypothesis that displacement of the tooth stimulates the periodontal end-rings, while deformation of the tooth stimulates the dentinal end-rings. It seems to us unnecessary to have to resort to van der Sprenkel's elaborate conception of both periodontal and intradentinal nerve-endings to explain the sensibility of teeth to pressure, especially as Stewart was able to show that the minimum stimulus required to get a response was very small. It is conceivable that such slight degrees of pressure would actually cause distortion of the tooth substance and so stimulate the intradentinal end-rings of van der Sprenkel. It is true, of course, that the forces of mas-

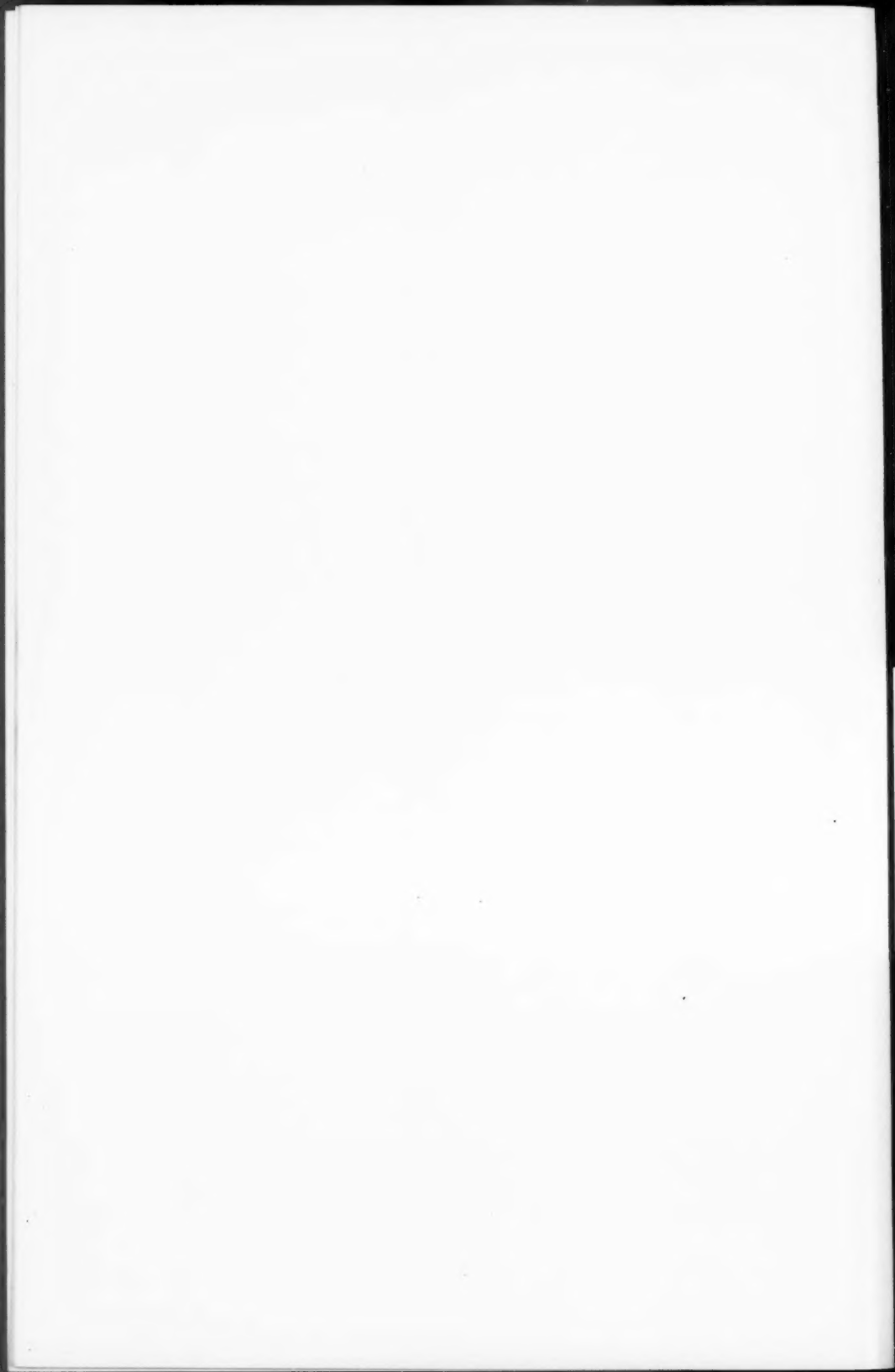
tication might cause such a distortion, but even here, surely the end-organs in the periodontal membrane would be sufficient without postulating a second series of end-organs in the dentine. It is well known that the periodontal membrane also reacts to painful stimuli and we suggest that the two types of nerve-endings that we have observed are probably associated with pressure and pain.

Acknowledgments

The authors wish to thank Professor Stopford for his permission to use all facilities in the Anatomy Department. To Mr. Gooding we are deeply indebted for his technical assistance and the excellence of the specimens is largely due to his skill. We have to express our thanks to Miss J. Dobson who has been of great assistance in preparing this paper for the press.

REFERENCES

- BLACK, G. V. (1887), "The Periosteum and Peridental Membrane", Chicago.
 BOEDEKER, C. F. W. (1883), in Heitzmann's "Mikroskop. Morphologie der Tierk.", pp. 628-633.
 BRADLAW, R. (1936), *Proc. Roy. Soc. Med.*, **29**, 507 (Sect. Odont., 27).
 BRASHEAR, A. D. (1936), *J. Comp. Neurol.*, **64**, 169-183.
 CZERNIAK, J. N. (1850), quoted by van der Sprekel, 1935.
 DEPENDORF, T. (1913), *Deutsche Monat. Zahnheilk.*, **31**, 853-864.
 HOPEWELL-SMITH, A. (1919), "Normal and Pathological Histology of the Mouth", Vol. I, London.
 HUBER, G. C. (1899), *Dental Cosmos*, **11**, 797-811.
 KADANOFF, D. (1929), *Verhandl. d. phys.-med. Gesellsch.*, **54**, 27-32.
 LEWINSKY, W., and STEWART, D. (1936), *J. Anat.*, **71**, 98-102.
 Id., 1937, *ibid.*, **71**, 232-235.
 LINDERER, C. J. (1837), *Handb. der. Zahnheilk.*, Berlin.
 OCHOTERENA, I. (1933), *An. Inst. Biol.*, **4**, 71.
 RETZIUS, G. (1894), *Biol. Untersuchungen*, n.f., **6**, 40.
 SICHER, H. (1928), *Fortschr. Zahnheilk.*, **4**, 255-271.
 SPRENKEL, B. VAN DER (1935), *Rev. Odontol.*
 Id. (1935), *Ztschr. f. mikr.-anat. Forsch.*, **38**, 1-86.
 Id. (1936), *J. Anat.*, **70**, 233-241.
 STEWART, D. (1927), *Proc. Roy. Soc. Med.*, **20**, 1675 (Sect. Odont., 55).
 WEDL, C. (1870), "Pathologie der Zähne mit besonderer Rücksicht auf Anatomie und Physiologie", Leipzig.
 WINDLE, W. F. (1927), *J. Comp. Neurol.*, **43**, 347-356.
 WOOLLARD, H. H. (1936), *J. Anat.*, **71**, 54-60.

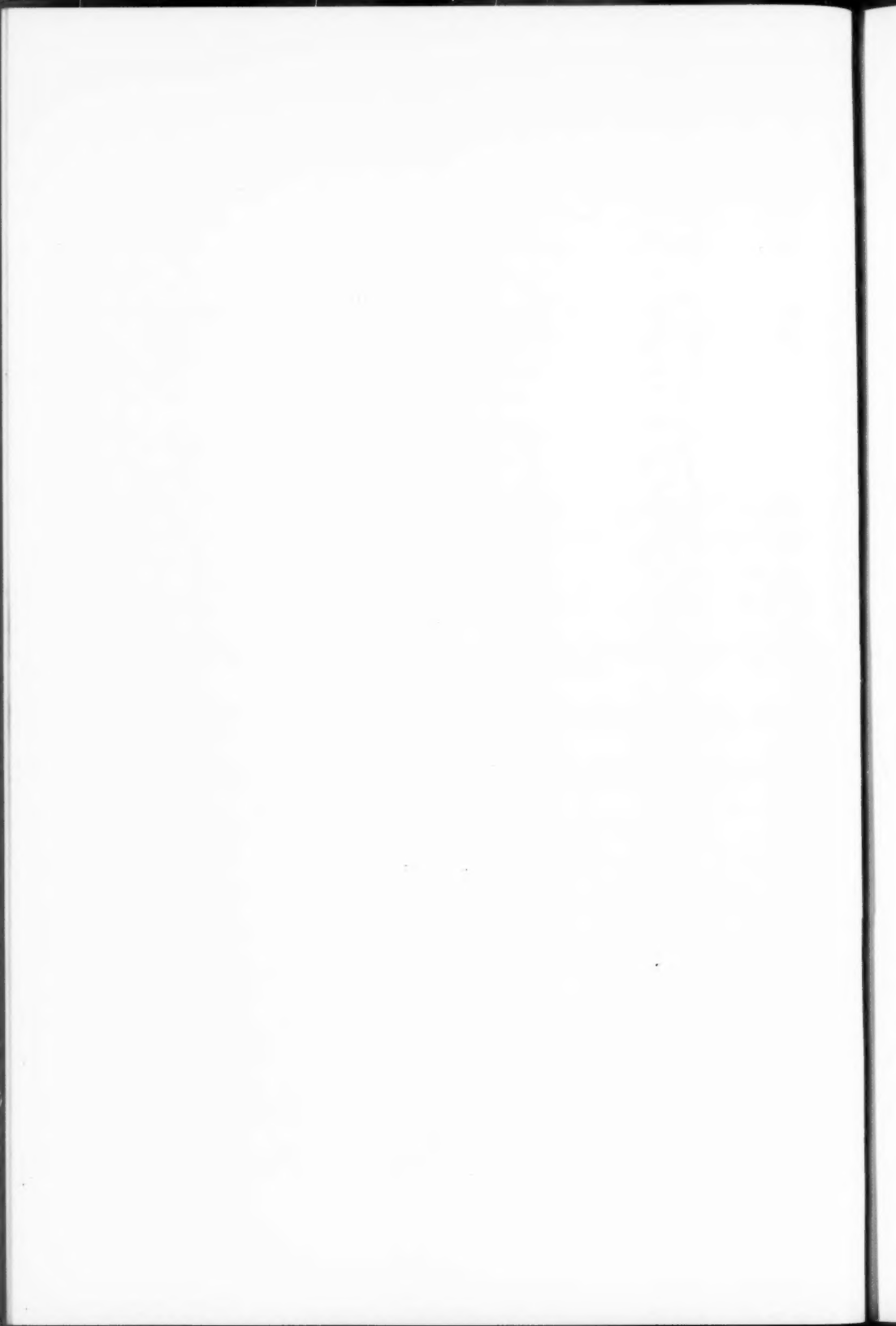


ERRATA

The following were Press errors in—

Vol. 30, p. 782 (Section of Radiology, p. 10)

- (1) Third line from top of page: *For* "microscopic" *read* "macroscopic".
- (2) The paragraph marked (3) should be read *after* that beginning "Histological examination . . ."
- (3) In the second reference (p. 24), after *Brit. J. Radiol.*, insert 10, 171.



Section of Radiology

President—DOUGLAS WEBSTER, M.D.

[April 16, 1937]

DISCUSSION ON SOME OF THE LESS COMMON LESIONS AND SPECIAL METHODS OF INVESTIGATION OF THE ALIMENTARY TRACT AND THE INFLUENCE OF ADJACENT ORGANS

Dr. Courtney Gage: It is not possible in the time available, for me to do more than touch on some of the various lesions I have selected, and I propose to include only those that have come, at least to some extent, under my own personal observation. Three, however—sarcoma of the stomach, paraduodenal hernia, and Crohn's disease—claim, and will receive, rather more attention. I shall give no statistics except in so far as they may be an aid to diagnosis, and shall attempt no exhaustive description. The general characteristics and diagnostic features will be well known to you all, but I hope here and there to stress any features peculiar to, or conspicuous in, the cases I shall present, and perhaps here and there suggest a possible diagnostic feature for your consideration, acceptance, or rejection.

SARCOMA OF THE STOMACH

This is a relatively rare condition, and nearly everywhere, when a single or a series of cases is reported, it is stressed that clinical and radiological differentiation from carcinoma is impossible, but with this I beg leave to disagree in one particular, because there is one type—the pedunculated or semi-sessile myosarcoma—in which I think the X-ray features are characteristic. It is fortunate, too, that this is also the type in which the prognosis is excellent.

In the other types it will matter little to the patient, at the present time, whether they are differentiated from carcinoma or not, as the prognosis is very much the same in both—but perhaps a little better in sarcoma, because dissemination takes place later and surgical removal is, on the whole, somewhat easier. However, for my purpose, I must divide even the myosarcoma into two groups:—

- (1) Those that protrude into the lumen of the stomach.
- (2) Those that make their way towards the peritoneal surface, protrude on the outer gastric wall, and do not affect the mucosa at all, but deform and displace the

stomach after the manner of an extrinsic tumour. These subperitoneal tumours tend to be clinically silent for a long time, even when large, and they may give rise to no definite symptoms until secondary deposits appear, or necrosis or some other complication arises. It will be worth while to keep this type in mind as a possible cause of gastric deformity and displacement, when there is nothing to implicate any of the adjacent organs as the cause.

There are certain generalizations which can be made about sarcoma of the stomach as a whole, clinical and pathological features which should be permitted to have some bearing on the radiological interpretation: isolated they are of little value, co-ordinated they may establish an unexpected but correct diagnosis.

There are, unfortunately, very few radiographs available for study, but surely we can infer much of what we may expect to see in a radiograph from such specimens and photographs of specimens as are available.

The youngest recorded case is, I believe, 8 years and the oldest over 80 years. The peak age-incidence of onset is round about 40 years, but lymphosarcoma (Plate 1B) occurs more frequently in those below this age. The sex incidence is about equal. The site is of some importance and of definite diagnostic value, because it is very rare to find the growth situated at the pylorus or at the cardia, therefore, neither oesophageal nor pyloric obstruction is to be expected.

It shows a very marked tendency to originate close to the lesser or greater curvature—not directly on the curvature, but it does, of course, encroach on the curvatures as it increases in size. These sarcomata as a whole are prone to central necrosis, and when multiple necrotic foci are present they give rise to a cystic appearance, so that the surface of the tumour may become grossly nodular.

Ulceration of the mucosa is less common than in carcinoma, and bleeding is rare. Some are very big—much larger than any conceivable gastric carcinoma—and may weigh several pounds. Pain is sometimes a prominent feature, as compared with that in carcinoma, but cachexia and anæmia are less marked, in relation to the size of the tumour or the area of gastric involvement. I have said that bleeding is rare, and this is true, with one exception—that of the myosarcomata which protrude into the gastric lumen. In these, bleeding and secondary anæmia may be the only clinical features. It is this group that presents the typical radiological picture to which I referred earlier, and they are by far the most important—to the patient, because cure can be effected by surgical removal, and to us, because the responsibility for diagnosis rests with us. I believe that a definite diagnosis can be made in nearly every case, and the post-operative prognosis is excellent. The degree of malignancy is very low: local infiltration, glandular involvement, and metastasis, are all extremely rare, but bleeding is a very prominent and serious feature, and it is only the severe anæmia that makes the operation hazardous. There may be no symptoms to point to the stomach as the source of the bleeding which is leading to progressive and fatal anæmia or hæmorrhage.

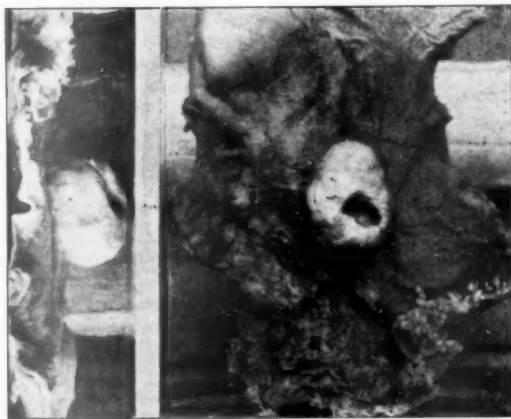
In shape, they are a slightly squashed sphere; a tangerine gives a perfect mental picture: the dimple of the stalk-attachment indicates the common site of the necrotic ulcer. These tumours may have a very definite pedicle or they may be semi-sessile; however sessile, the greater diameter of the tumour will be larger than the base, as distinct from carcinoma, in which the infiltration will usually extend beyond the tumour base. It will be situated close to the lesser or greater curvature, usually the former.

Central necrosis and rupture through the mucosa over the tumour give rise to a single central deep ulcer from which the bleeding occurs. The proximity of the tumour to the curvature, particularly the lesser curvature, permits the imprisonment of barium between the tumour and the gastric wall in such a way that it will give a quite distinctive X-ray appearance. If there is a definite pedicle, peristalsis will

continue uninterrupted over the attachment; if semi-sessile, it will go right up to the base of the filling defect, an area smaller than the greater width of the tumour. There is no rigid zone surrounding it, the rugæ will be pushed away on either side and such rugæ as would normally cross the centre of the tumour area will be smoothed out over the tumour—for it must be remembered that the mucosa is not an elastic structure. If seen before the formation of a necrotic ulcer, the mucosa will be smooth and regular.

I have illustrations from two such cases to show here. One (Plate Ia) is the case already reported by Dr. Thomas Hunt and myself in the *Brit. J. Radiol.*, 1932, N.S. 5, 718.

This case was successfully operated upon by Professor Pannett after several blood transfusions, and the patient is now quite well.



FIGS. 1 and 2.—Case II. Specimen of myosarcoma, showing characteristic semi-sessile tumour with necrotic ulcer in the middle. Lateral view shows an ulcer on the surface and its pedunculated base. (Dr. Adolphe Abrahams and Dr. Rickword Lane.)

The second (figs. 1 and 2) was admitted in a desperate condition to the Hampstead General Hospital under Dr. Adolphe Abrahams. The patient died from hæmorrhage before anything could be done, in spite of several blood transfusions.

POLYPOSIS OF THE STOMACH

This term is very elastic, being used to describe a wide variety of pathological changes, which range from the coarse granular appearance of closely packed elevations to large grape-like masses with fully formed pedicles. It is impossible to know what mental picture the term is intended to convey, unless it is elaborated.

The cases from which I am showing illustrations are of the multiple grape-like type, and to this type only applies the diagnostic point I wish to submit for consideration.

I would draw attention to the decreased size of the fundus. I have thought that these polypi, now massed towards the pyloric end, were earlier, more evenly distributed

over the gastric surface and that the passage of food and peristalsis has produced a definite drag on the fundus and even a mucosal shift towards the pylorus. However I will let the radiographs (Plate IC, D) and the specimen speak for themselves.

RETROPERITONEAL HERNIAS (Plate IIA, B)

(More particularly hernia into duodenojejunal fossæ)

Fossæ into which hernia may occur have been described both in the cæcal region and about the sigmoid, but they are even less common than those in the region of the duodenojejunal junction. These latter are, I believe, more frequent than the number of published cases would indicate, and if my own experience is anything from which to judge, I would suggest that many of those of minor degree escape detection as the cause of symptoms and of duodenal ileus.

These hernias vary tremendously in size; almost all the small intestine may be included, or only a very small segment. Sometimes only a small knuckle is tucked in not including the whole circumference of the gut. These I classify in my own mind as of the "Richter type", and they may easily be mistaken radiologically for a diverticulum.

Para-duodenal hernia was recognized and described as far back as 1742. The first comprehensive study, however, was that by Lord Moynihan, published in 1899, and it remains to this day the monograph on the subject. Moynihan describes nine fossæ in this region, several of which appear to be of academic interest only, and not of major importance.

The detailed anatomy is important to the surgeon, on account of the different vascular content in the borders of some of the fossæ, but I shall not describe any of them, not only because time does not permit, but because I think they can be radiologically differentiated. Some of the fossæ are formed by the raising of the peritoneum by blood-vessels, others by the failure of the root of the mesentery to unite with the posterior wall of the abdomen.

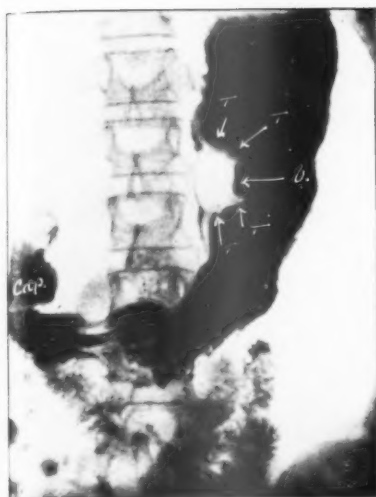
The size of the hernia bears no relation to the symptoms; both the very large and the very small may be symptomless, or practically so, until some degree of obstruction occurs—ranging, according to the severity of the obstruction, from occasional attacks of colic to an abdominal emergency.

When acute obstruction occurs a barium examination is out of the question. In a simple examination, only two fluid lines are to be expected, the normal one in the stomach, and the pathological, in the distended duodenum. The latter may be hidden by the former and missed entirely unless a special film is taken to show the duodenum. Every case of duodenal ileus extending to the left of the mid-line should be regarded as probably of serious import, and should be investigated in detail. I have had no personal experience of these very large hernias, but Mr. E. Dowdle's case report of a "right para-duodenal hernia" in *Surg., Gynec. and Obst.*, 1932, 54, 246, is, I think, of great interest.

These large hernias present an X-ray appearance of "massing" of the small intestine, which really suggests that the gut is contained within a bag. At the right lower border the edge of the shadow of the small intestine mass presents an almost unbroken convex line. The quite small hernias may show nothing more than stasis in a small knuckle of gut at the duodenojejunal junction, and a few will be found radiologically in patients who are symptom-free, nevertheless, their recognition may be a matter of vital importance.

The differential diagnosis from a diverticulum presents no great difficulty. The site is not a common one for a diverticulum, there is no stalk, and the base is flat and

PLATE I



A



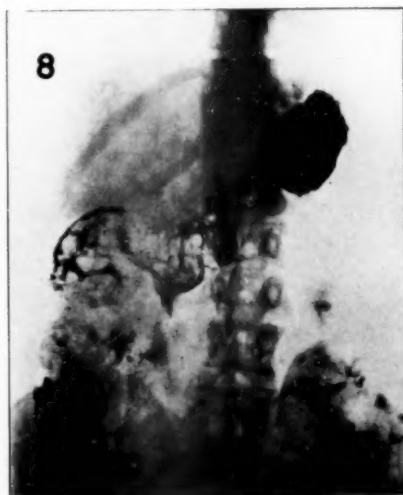
B

(A) Myosarcoma, showing a typical filling defect due to the tumour, and the ulcer crater in the tumour.

(B) Lymphosarcoma, showing close similarity to the appearance of carcinoma. Note, however, that neither of the curvatures has been encroached upon.



C

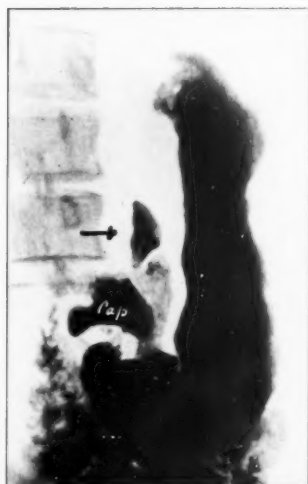


D

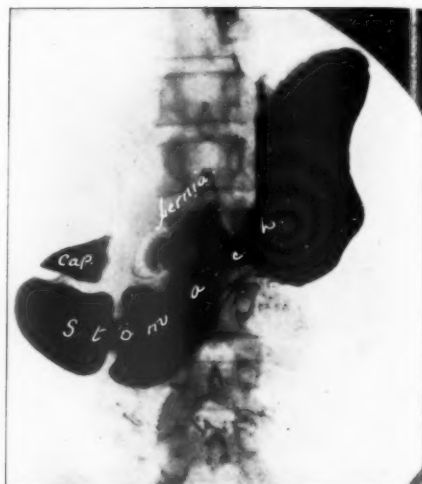
(C and D) Polyposis of the stomach. Note small size of fundus, ? due to drag of polypi towards the pylorus by food and peristalsis. (C, erect, D, prone.) (Mr. Cope and Professor Newcomb.)

COURTNEY GAGE: *Some of the Less Common Lesions and Special Methods of Investigation of the Alimentary Tract and the Influence of Adjacent Organs.*

PLATE II



A

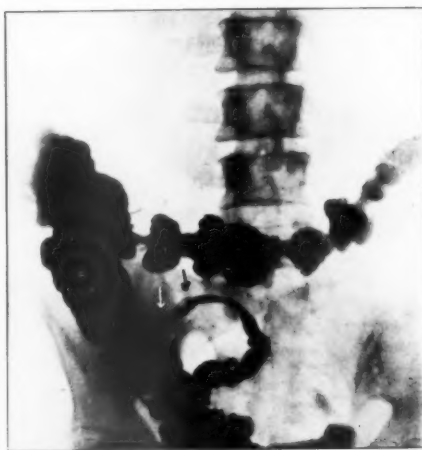


B

(A) A small para-duodenal hernia showing half "wiped-out" appearance.
(B) A rather larger hernia passing over to the right.



C



D

(C) Annular carcinoma of the third part of the duodenum with compression. (Dr. Brock's case, 1931)
(D) Crohn's disease. Stenosis of the terminal ileum showing marked serrations along the mesenteric border of the bismuth shadow and obstruction in the ileum proximal to this.

COURTNEY GAGE: *Some of the Less Common Lesions and Special Methods of Investigation of the Alimentary Tract and the Influence of Adjacent Organs.*

wide. There is usually a linear half-shadow within the barium shadow (the barium density is not uniform as it is in a diverticulum), but it shows a partially wiped-out appearance of a smooth graduation. When there is barium in the adjacent gut, the gut line is seen to be continuous; it is fixed and constant.

I would refer those who may be interested in the contrasted clinical features of the "acute abdominal emergency" type to two cases operated on at St. Mary's Hospital, by Mr. Arthur Porritt, both patients had an uneventful convalescence. An account of these two cases will be found in the *Lancet*, 1934 (ii), 1156.

PRIMARY CARCINOMA OF THE DUODENUM (Plate IIc)

This is very rare and must not be confused with the much more common duet carcinoma, which frequently spreads to the duodenum.

An illustrative case is reported as follows :—

The patient, a woman aged 67, was first seen 11.6.31 in consultation with Dr. J. H. E. Brock. Past history of no interest; no previous dyspepsia. Had been sick after food three times during the previous month. No blood. No melena. Some upper abdominal discomfort. Nothing to be felt in the abdomen. Patient attributed the upset to the smell of paint in the house.

25.6.31: Vomited again; still no pain after food, but very bitter taste after vomiting. The dyspepsia improved on alkalines, and belladonna, and modified diet, but occasional vomiting persisted.

2.11.31: Tender spot up under the left costal margin; stomach pylorus, gall-bladder and appendix regions nil abnormal. No hæmatemesis, or melena. Appetite still good. Now constipation and loss of weight.

5.11.31: X-ray examination: A large stomach of quite good tone, normal peristalsis but slight delay in the emptying time. There is no evidence of any organic lesion of the stomach, and the duodenal cap is normal. There is a filling defect in the third part of the duodenum, with stenosis and duodenal ileus.

Diagnosis.—Annular carcinoma of the third part of the duodenum. Nothing abnormal to be felt in the abdomen.

6 and 7.11.31: Patient vomited large quantities of bile-stained fluid.

9.11.31: Dr. Brock was called urgently to this patient at 8.45 p.m. She was thought to be dying, she was in a severe attack of tetany. Morphia was given hypodermically and a bromide and chloral enema in 5% glucose. She was soon relieved and had a comfortable night.

13.11.31: Mr. Gwynne Williams aspirated the stomach contents and obtained only 4 ounces of bile-stained fluid; at the operation the first and second parts of the duodenum were seen to be quite healthy, but a carcinomatous stricture was found in the third part of the duodenum.

CROHN'S DISEASE (Plate IID; Plate IIIA)

I think it is highly probable that there is no one more surprised that there is such a thing as Crohn's disease than Dr. Crohn himself.

The condition had no doubt been observed many more times than the isolated published cases would lead us to believe, but published, as they were, under varying descriptive titles each one came to be regarded more or less as a medical curiosity, until in 1932 Dr. Crohn and his co-workers published their series of cases, and established the disease as a definite clinical and pathological entity.

The descriptive titles include amongst others "regional enteritis", "chronic hypertrophic ileitis", "chronic hyperplastic enteritis", &c., &c.

It is not easy to find an adequate short descriptive name because, although the common site is in the terminal part of the ileum, it is not confined to this segment and may occur elsewhere in the ileum, and in the jejunum; and it has been described in the colon. It may be a single lesion or multiple. "Non-specific chronic inflammatory granuloma of the intestine" appeals to me as the best descriptive title at the moment, but it is long and cumbersome; "non-specific" is used in its widest sense, that is to say, excluding tuberculosis, actinomycosis, syphilis, and Hodgkin's disease.

However, "Crohn's disease" is a short name which has served to focus attention on the disease as an entity, and since 1932 the literature has bristled with both isolated and collected series of cases. There can be little doubt, that in the past, what some have thought to be a somewhat typical ileal tuberculosis was in fact Crohn's disease, and that in the present period of enthusiasm the reverse may also be true. This condition of non-specific inflammatory granuloma is an inflammatory condition of unknown aetiology. It occurs most frequently in young adults, but it has been reported in patients as young as 5 and as old as 61. It occurs more frequently in males than females.

When it occurs in the terminal ileum it usually ends abruptly at the ileo-cæcal valve; elsewhere it may end abruptly or fade off into normal gut. It may involve a long, or only a short, segment of the gut. The part is increased in size, usually to about one and half times the normal diameter and presenting the appearance of a sausage-like tumour, red-to-purple in colour, rather rigid and firm to the touch. The thickening and enlargement are perhaps most simply described as due to granulation-tissue formation throughout all layers of the gut wall. The mucosa is swollen and the folds thickened, sometimes narrowing the lumen to such a degree as to cause severe obstruction.

If ulceration of the mucosa occurs it does so along the mesenteric border, and should perforation follow, it will take place into the mesentery and from there into other coils or the colon, usually into the sigmoid.

External fistula is a complication that may arise following the draining of an abscess, the true nature of which may not be suspected. If several coils are affected, or if there are complications, such as a mesenteric abscess with or without an entero-enteric fistula, there may be a quite large palpable tumour. The clinical picture is variable and will be coloured by the site of the lesion and the balance between acute, subacute, or chronic inflammation, and acute, subacute, or chronic obstruction. The disease occurs so much more frequently in the terminal ileum than elsewhere, that in most of the cases the abdomen will be opened on account of an acute or subacute inflammatory lesion in the right iliac fossa, and appendicitis will be the provisional diagnosis in most cases. It will be the more chronic cases which have progressed to a definite degree of obstruction and those with pain and a palpable tumour or those with fistula formation, which will become the subjects of radiological investigation.

The radiological signs of chronic obstruction of the small intestine must all serve in this, as in obstruction from any other causes. To this we must add what has in this connexion been termed the "string" sign, the thin ragged line of barium to be seen within the narrowed lumen of the stenosed section of the gut. This sign, however, is not conspicuous in the case illustrations that are available for inspection, neither is it to be expected if a routine barium-meal examination only is employed, because it makes no provision for the motility, mobility and distribution peculiar to the small intestine. The examination of the small intestine demands a special technique. (Plate IIIA.) We may now well ask if there is any special feature which might possibly give a distinctive sign should we be able to develop a technique to show it. I think there may be one and if so it will, I think, be due to the peculiar tendency to linear ulceration of the mucosa along the mesenteric border and the tendency to perforation into the mesentery. Such facts of pathology, if they are

PLATE III



A



B

(A) Crohn's disease (Mr. Sidney Boyd's case). Two small strictures are seen in the short-circuited section of the intestine, with distension between them. Upper stricture shows a well-marked protrusion of barium towards the mesenteric border. (This film is one of a series taken with special technique for the small intestine.)

(B) Mr. Cokkinis's case. The barium was contained in a pocket formed by the intercommunication of two or three coils of the jejunum due to ulceration through the walls. (Specimen shown by courtesy of Professor Newcomb.)



(C) *Ascaris lumbricoides*. A, worm. B, stool of worm.

COURTNEY GAGE: *Some of the Less Common Lesions and Special Methods of Investigation of the Alimentary Tract and the Influence of Adjacent Organs.*

PLATE IV

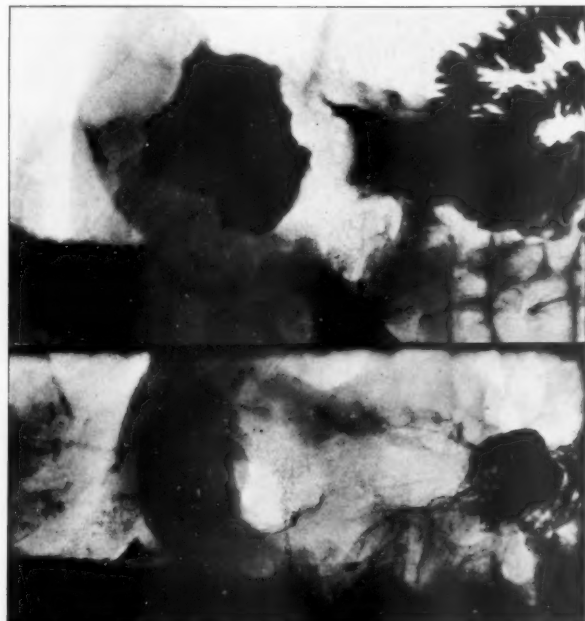


FIG. 1. A B

(A) Encephaloid carcinoma of the gastric fundus outlined by the gas bubbles in the erect position.

(B) The same, outlined by barium, in the supine position.

FIGS. 2 AND 3.—Visceroptotic woman. Barium meal, patient supine. Fig. 2 shows posterior (pancreatic) incisura of Twining. Fig. 3, lateral view, shows the incisura surmounting a triangular filling defect due to the normal pancreas.

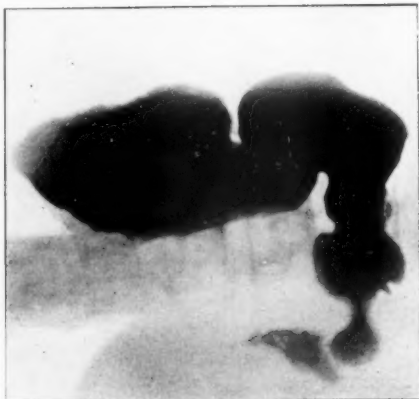
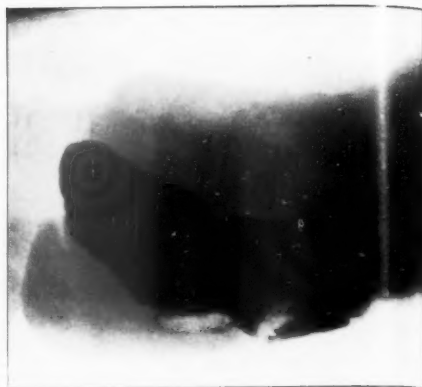


FIG. 2.



facts, should lead us to direct our technique in such a way as to secure the best possible filling of the lumen that we may by skill or artifice obtain, unobscured by massing of the other loops of the gut, and then manipulate the segment so as to bring the mesenteric border into profile.

The pathology would lead us to expect serrations and projections of barium of a shape and length peculiar to the mesenteric border of the gut. Other features will contribute something to the whole that will give the diagnostic data for a given case, and I submit the following for your criticism.

A search through the literature shows that adhesions are not very common, and this still applies even when there is a mesenteric abscess present. I would, therefore, suggest that fixation will be a strong point in favour of some other lesion.

The thickened gut may be freely angulated on the caecal wall, or made to indent it locally, proving the flexibility of the caecal wall and demonstrating its freedom from involvement.

ASCARIS LUMBRICOIDES (Plate IIIC)

Female : 8 to 10 inches long. Male : 4 to 8 inches long.

Filling defect 4 to 8 millimetres wide.

Single often means a bachelor male.

Life cycle. Ova ingested on salads, and hatch in small intestine. The larvæ migrate through the wall of the intestine and enter the vascular system, and ultimately reach the capillaries of the lungs. They develop in the alveoli. They may give rise to pulmonary changes, they then pass up the bronchial tree and are swallowed. After leaving the lungs they take about six weeks to mature.

Technique: No food overnight, cereal meal; film hourly from one hour afterwards.

Large whorled masses are seen, with barium between them or thin lines of barium within the gut.

It is very important to recognize the radiological evidence of the presence of these worms—not only the large masses, but also the isolated single worm. The former having once been seen will not be missed on a second occasion, but the latter, showing only a thin line of barium within its intestine when full, or the stool when it has been evacuated, is very easily missed or disregarded if its significance is not appreciated.

The parasite may give rise to symptoms simulating tuberculous peritonitis, duodenal ulcer, carcinoma of the intestine, gall-bladder disease and liver abscess, or may cause obstruction. The single worm may be the cause of obscure cases of vomiting and loss of appetite.

It gives me great pleasure to express my gratitude to my colleagues, physicians and surgeons, for their co-operation in the investigation of these and other cases, to Professor W. D. Newcomb for his help, and loan of four specimens (myosarcoma, polyposis of the stomach, diverticulum of the stomach and Crohn's disease) and to Dr. Rickword Lane for his help and loan of specimens of carcinoma of the stomach and myosarcoma of the stomach.

Dr. S. Cochrane Shanks: The subject of unusual methods of examination of the alimentary canal is rather difficult of approach, since unusual methods are usually experimental, and it is difficult to assess their value. Each has its vogue, and later may find its sphere of usefulness, or disappear into the limbo. I propose to mention several which appear to have some inherent value and to comment on my rather limited experience in some of them.

THE PHARYNX, ŒSOPHAGUS, AND STOMACH

The Pharynx

I should like to mention the value of the true lateral view, without the use of any contrast medium, and exposed so as to show the soft parts, in the examination of the hypopharynx. Air then forms the contrast medium, and full distension of the lower pharynx is very simply achieved, by asking the patient to blow his nose steadily and firmly during the exposure. This separates the anterior and posterior pharyngeal walls, and a tumour mass projecting into its lumen may be clearly seen.

The Œsophagus

A useful variant of the orthodox erect position in examining the œsophagus is the right oblique view, with the patient prone or in the Trendelenburg position. This, when combined with the double-swallow method, outlines the lower as well as the upper limits of a stenosis, and often gives more information than examination in the erect position.

It has its use also in showing a traction diverticulum of the œsophagus, which may not fill with the patient standing.

The Trendelenburg position is essential in examination of diaphragmatic hernia of the stomach and congenital thoracic stomach. Dunhill recently emphasized this, and pointed out the characteristic differential features of the œsophagus in these two conditions. The exact posture necessary to separate the œsophageal and fundal shadows in these cases cannot be laid down. Each case is a law to itself; prone, supine or oblique views may be necessary, and the one requisite in any particular instance can be determined only by fluoroscopy. One difficulty is that the picture changes with peristalsis: what was a clear fluoroscopic view may be overlapped in the subsequent radiogram, and repeated examination and much patience may be necessary before a successful picture is produced. Such cases may be very time-consuming, as are, indeed, several of the special examinations I shall mention later.

The mucous pattern of the normal œsophagus may be difficult to demonstrate with certainty, either with barium-tragacanth or barium-water, or the thorium preparations. Of the latter, diathorine, which flocculates, should, in theory, work, but I have not found it satisfactory. Possibly, peristalsis is too active to allow a sufficient deposit to take place.

For œsophageal varices a thick barium-water cream is best, and in this condition the deep interstices readily retain the barium.

The Stomach

The study of the gastric mucosa is now a routine measure, and requires no description here, but there are a few points I should like to mention.

The first is the medium. I have been disappointed with diathorine, which is very uncertain in its action. It sometimes gives a satisfactory pattern, but more often a blotchy appearance. This is to be expected, since any resting-juice coagulates the medium. My impression is that a thick colloidal barium-water cream is better than the usual tragacanth suspension. It mixes better with resting-juice than the latter, and, I think, gives a better coating. The formula I use is: kaylenema barium, three parts; water, two parts. Not more than half an ounce should be given, for Berg's dictum, that "the less you give the more you see", is undoubtedly true.

Prone and supine radiograms should be taken, after the patient has lain for some seconds prone, supine, and on each side.

Air inflation of the stomach.—Duval and Bécère find this method of value in the study of the mucous pattern. They use an Einhorn tube, first for emptying the stomach of resting-juice, and then for inflation. The latter is carried out under

fluoroscopic control. The value of this method is enhanced when combined with a barium whitewash or double contrast method.

Blind inflation, by a Seidlitz powder, suffers from the disadvantage that the inflation cannot be controlled and that fluid is introduced at the same time.

The authors claim that the method is of value in cases of encephaloid carcinoma and gastric polyposis, but that the risk of perforation contra-indicates its use in gastric ulcer. My own opinion is that it does possess a limited field of usefulness, in gastric polyposis and fundal tumours, but that in the latter case the normal gas-bubble is usually sufficient to outline the tumour (fig 1, Plate IV).

I have tried thorium instead of barium in this method, with the same disappointing results as in the plain mucosal pattern picture.

Abolition of gastropasm and duodenospasm.—According to Myerson and Ritvo (1936) benzedrine sulphate, in a dose of 10–30 mgm. by the mouth, relieves gastropasm and duodenospasm in 85% of cases. If these claims are true, it should be a useful method in differentiating between the spastic and organic elements in hour-glass stomach, in examining a cascade stomach, and in eliminating bulbar spasm in duodenal ulcer. It is also said to be effective in the treatment of colospasm.

Pitressin (10 units— $\frac{1}{4}$ c.c.) may be of value in biloculation of the stomach due to gas in the colon, by deflating the latter.

THE PANCREAS

This organ is difficult to examine radiologically, and a variety of methods may be necessary, depending on the lesion in question. They are :—

(1) *The plain postero-anterior film*, which will show pancreatic calculi, and in acute pancreatitis may show, according to Haring (1933), blurring of the shadow of the left psoas muscle.

(2) *Fluoroscopy* of the lung bases and diaphragm should be carried out if an acute pancreatitis is examined radiologically.

(3) *The barium enema* may give evidence of steatorrhœa in chronic pancreatitis.

(4) *The barium meal*. This may show a gastric or duodenal pressure deformity.

Dr. Twining, in a personal communication, has kindly supplied me with the details of the method he uses, and the differential points between the normal and the abnormal.

He radiographs the stomach, well-filled with barium, in the lateral (dextro-sinestral) view, with the patient supine. He has, I think, made important observations in the normal subject, in particular regarding what he calls the posterior (pancreatic) incisura, to which I should like to refer.

This anatomical variation, which occurs chiefly in ptotic women, varies according to the position in which the subject is examined, as follows :—

(i) Postero-anterior view erect : ptosis only is seen.

(ii) Postero-anterior view supine : an incisura develops on the posterior gastric wall, at the level of the pancreas, deepest at the greater curve (fig. 2, Plate IV).

(iii) Antero-posterior view prone : the incisura disappears.

(iv) Lateral view supine shows the incisura on top of a triangular filling defect due to the body of the pancreas itself (fig. 3, Plate IV). The incisura itself is due to an infolding of the gastric wall at the pancreas, and the recognition that there is a normal pancreatic filling defect is of importance in assessing the presence or absence of one due to a tumour of the pancreas or stomach-bed.

(5) *Air-inflation.*—Åkerlund, and Engel and Lysholm, use lateral radiograms taken in the prone position with air inflation, to show pancreatic tumours; the latter writers recommend inflation, via an Einhorn tube, followed by immediate radiography, before any of the gas has had time to pass into the duodenum. Gas in that site may obscure the picture. It is important, with this technique, to

relieve pressure on the abdomen by supporting the chest and pelvis on flat pillows or pads. Engel and Lysholm (1934) state that with a tube-film distance of 100 cm. (40 in.), the average normal pancreatic space, equals the width of the adjacent vertebral body.

I think Twining's method is the better of the two, since it avoids the use of the Einhorn tube, and because barium is a better contrast medium than air. In large tumours the Scandinavian technique might be used with barium as the medium, instead of air.

THE SMALL INTESTINE

In most cases the ordinary routine barium meal gives a satisfactory picture of the upper part of the small intestine, if the patient is examined prone. There is, however, an undoubted tendency for the ileum to become rather densely filled, and the contours of the individual coils obscured by each other. This may be a serious drawback in examining cases of ileal tuberculosis and Crohn's disease. I am indebted to Dr. Courtney Gage for details of a technique that he has devised which avoids this disadvantage, and the essence of his technique is to give a small barium-water suspension and to keep the patient in the prone position throughout the entire examination.

The details are as follows:—The patient should first empty the bladder. A small meal—not more than 4 oz. of a plain barium-water suspension—is given. The object of this small amount is to prevent overloading of the ileal coils. If 4 oz. proves to be insufficient, subsequent small feeds of about an ounce may be given during the examination until the small intestine is adequately outlined.

The patient is then placed prone on a pole canvas stretcher, and must remain in that position during the 5 to 6 hours of the examination. This position, if maintained, tends to produce an even distribution of barium throughout the small intestine, and to prevent it collecting in a heavy mass in the pelvic coils of ileum. The patient is lifted on to the X-ray couch on the canvas pole stretcher, and fluoroscopic palpation can be made by raising the poles on sandbags.

The first radiogram should be taken an hour after taking the meal, and at subsequent intervals of 1 to 1½ hours. They should be taken in full expiration. Occasionally, double exposures on one film at an interval of ½ to 2 minutes may be useful, to test the constancy of any irregularity of contour. The patient should not breathe deeply during the investigation, and no ordinary food is allowed till the examination is finished. The bladder should be allowed to fill during the examination, since a full bladder may help to prevent the ileum sinking into the pelvis.

Since the maintenance of the prone position for so long may be irksome to the patient, every means should be taken to make him as comfortable as possible in it.

The investigation of fluid levels.—There are many causes of fluid level in the abdomen, such as air-swallowing, cascade stomach, hour-glass stomach, gastro-colic fistula, and residues from plain enemata. Some of these are of no consequence, but Patey a few years ago drew attention to the importance of such levels in acute intestinal obstruction. Patients suffering from acute obstruction cannot stand much in the way of manipulation, and should be examined in bed with a mobile ward unit. A lateral radiogram of the abdomen should be taken, using a Schonander grid, and with the patient in the dorsal decubitus. This view shows the levels clearly. If the patient's condition permits, he may be turned on his side, and with a similar horizontal disposition of the rays, a postero-anterior view may be taken. A straight antero-posterior view, with the patient lying on his back, may give a rough idea of the site of the obstruction, if the bowel above the obstruction is much distended with gas.

This lateral technique is also useful in cases of suspected perforation. Any free gas in the peritoneum is clearly visible between the anterior surface of the liver and the anterior abdominal wall.

In chronic intestinal obstruction similar fluid levels may, of course, be present and are easily shown in the screening stand. Occasionally a difficulty may arise in a high obstruction, e.g. at the duodenojejunal flexure, from the superimposition of the gastric fluid level on that in the duodenum. In such a case, a useful measure is to take a postero-anterior radiogram with the patient lying on his left side, again with the Schonander grid. In this position, the gastric fluid is spread out along the greater curve. It is therefore a long one, and near the left flank. The duodenal level, on the other hand, is short, being in the fourth portion of the duodenum, and somewhere near the line of the spine.

External faecal fistulae.—Dr. Courtney Gage has devised an ingenious method, which he calls the "ghost enema", of demonstrating small faecal fistulae involving the colon. The colon is filled *per anum* with a dilute barium-water suspension, just dense enough to outline the gut and transparent enough to make a dense medium, such as lipiodol, visible through it. The fistulous track is then injected with lipiodol. Tiny fistulae can be shown by this method, since even a few drops of lipiodol passing through the fistula are orientated in the faintly outlined bowel. To prove that these droplets are in the bowel and not in the track, the latter must be completely filled during the exposure. This is best achieved by using a Gibb's urethral syringe for the injection, and by keeping up the pressure whilst the exposure is made. Stereograms, taken with as short an interval as possible, are a further help.

Internal fistulae.—In examining the commonest and most systematized type—the gastro-colic, from carcinoma, and the gastro-entero-colic from post-operative jejunal ulcer—I much prefer the enema method. The flooding of the gastric fundus with a barium enema is quite conclusive. If the meal is used, the detection of barium in the colon within ten minutes is essential, for we have all seen barium reach the colon within half an hour after the ingestion of a meal. I have seen it twenty minutes after. Again, one must make quite certain that the colonic shadow is not due to bismuth previously taken by the patient. In this respect there is a distinguishing point; barium escaping into the colon through a tiny fistula first tends to coat the haustral pockets in a thin line if the colon contains faeces, whereas bismuth or barium which has arrived in the normal way forms the faeces themselves.

The evaluation of Stierlin's sign.—Stierlin's sign in hyperplastic ileo-caecal tuberculosis is supposed to be a spasm of the caecum and proximal ascending colon. It may, however, be due in some cases partly to spasm and partly to organic contracture from the disease process. It is wise therefore to follow the meal examination by a barium enema, in the later stages of which the spasm may relax and reveal any organic narrowing that may be present.

THE COLON

The available methods of radiological examination of the colon are the plain picture, the barium meal, the barium enema, the barium-air three-stage enema, and the thorium-air three-stage enema. It is of the last two that I want to say something; regarding the technique, what is claimed for them, and my own experience with them.

The object of both is the study of the mucous pattern: neither is always successful, but both certainly are successful in consuming much time. It is surprising how the search for a disorganized mucosa can also disorganize the afternoon's work in the department!

The Barium-Air Three-stage Enema

The technique of the barium-air enema is as follows:—

The preparation is all-important, and must ensure complete evacuation of the colon. Two ounces of castor oil on the day before, and on the morning of the examination; thorough colonic lavage. For this the Studa chair is undoubtedly the most satisfactory, if available. It may not be popular in hospital practice, since it

takes at least forty minutes to give a Studa wash-out efficiently, during which time a nurse must be in constant attendance.

The medium.—I can warmly recommend the use of colloidal barium suspended in plain water.

- (1) It is easy to make. All that is necessary is to add the requisite amount of barium (10 oz. to a pint) to warm water in a Winchester, and shake vigorously.
- (2) It is easy to clean the apparatus after its use.
- (3) It is cheaper than the standard emulsions.
- (4) It holds up in suspension for a reasonable time—half to one hour—and can be used in a comparatively dilute state. This has the advantage that superimposed coils of barium-filled gut can be to some extent differentiated.
- (5) It deposits on the mucosa more satisfactorily than the tragacanth emulsion does.

After the ordinary barium enema examination has been completed, the patient empties the bowel. A radiogram is then taken to show the mucosal pattern, if evacuation has been sufficiently complete. Frequently the pattern is not shown, but there is more chance of success in this respect if the plain colloidal suspension is used (fig 4, Plate V).

The colon is then inflated with a Higginson's syringe under radioscopic control. If too much barium remains the patient is sent to stool and the process repeated. Two or three evacuations may be necessary before the bowel is sufficiently empty. After the final inflation radiograms are taken; these may be stereoscopic with advantage. To obtain successful stereograms both exposures should be made as quickly as possible while the patient is holding the same breath (fig. 5 Plate V).

The Thorium Three-stage Enema

This a variant of the barium-air enema, and is also in three phases: (1) The filled colon. (2) The collapsed colon, showing the mucosa by flocculation of the opaque medium. (3) The inflated colon.

The labile colloidal aqueous suspension of thorium oxide has a greater tendency than barium to deposit itself on the colonic mucosa. Three preparations are available so far—collothor, umbrathor, and diagnothorine. Thorotrast, a stable suspension, does not flocculate, and is unsuitable for this purpose. Diagnothorine, the preparation which I have used, is a 25% colloidal aqueous suspension of thorium oxide. The type of flocculation depends on the pH of the colonic interior colon: a high pH is said to induce deposition of an elastic layer, while a low pH induces one less viscous and more apt to fragment. The colonic pH should be adjusted to the necessary value before the examination, and this is best done by lavage with 1 to 2% sodium phosphate.

Preliminary preparation.—Because of the biophysical factors involved, this is of the utmost importance. The colon must be completely emptied of all contents and mucus.

Maingot recommends the following:—

- (1) Castor oil, 2 oz., on the evening before, followed by a liquid diet.
- (2) On the morning of the examination, colonic lavage two hours before, and with the 1 to 2% sodium phosphate solution 1 hour before. Salines and drastic purges are to be avoided, as they irritate the colon and cause hyperæmia and hypermotility of its mucosa.

Technique.—The diagnothorine is diluted to about 8 to 10% with distilled water. Tap water causes immediate precipitation of the colloid, and must not be used.

First stage: The essential point is to use as little of the medium as possible; distension of the colon is to be avoided. About a pint should be enough to fill the colon; sometimes more is necessary. The injection is given intermittently, about 2 oz. at a time, by gravity or by a Higginson's syringe. Distension of the rectum is

PLATE V



FIG. 4.—Colloidal barium enema. Normal mucous pattern after evacuation.
S. COCHRANE SHANKS : Some of the Less Common Lesions and Special Methods of Investigation
of the Alimentary Tract and the Influence of Adjacent Organs.

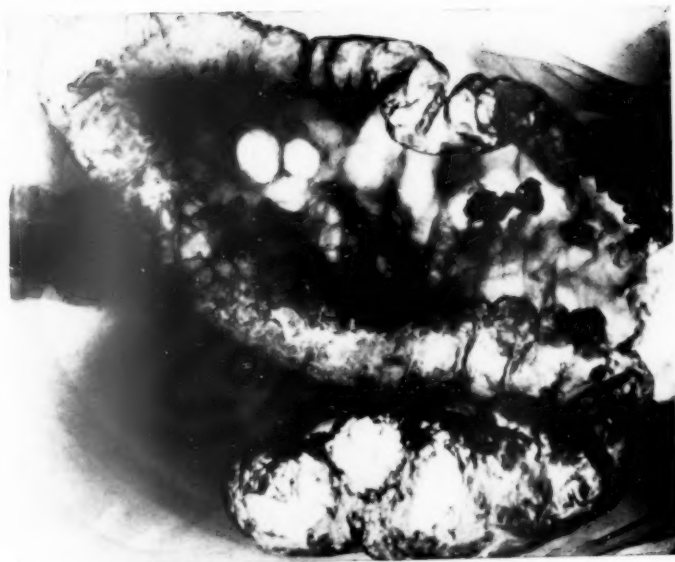


FIG. 5.—A case of mucous colitis. Barium-air double contrast enema, showing honeycomb pattern after inflation.

PLATE VI



FIG. 6.—Normal thorium-air enema, first stage.

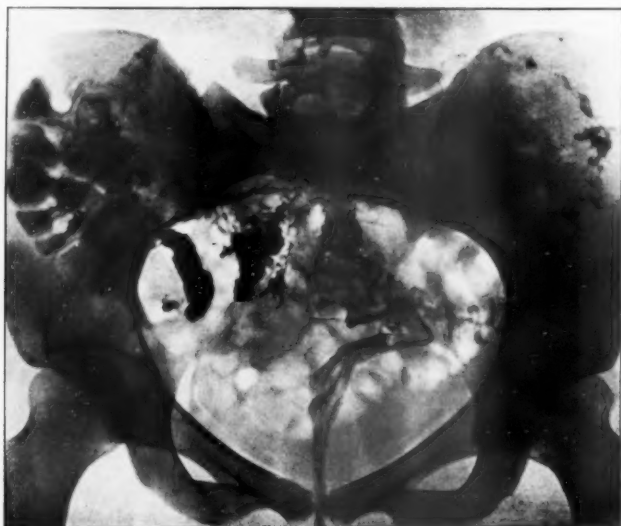


FIG. 7.—Normal thorium-air enema, second stage.

S. COCHRANE SHANKS: *Some of the Less Common Lesions and Special Methods of Investigation of the Alimentary Tract and the Influence of Adjacent Organs.*

to be avoided, if possible, since the rectum may not contract satisfactorily in the second stage, and so retain too much of the medium. Usually the colon fills as far as the mid-transverse colon, but it may be difficult or impossible to fill the right colon. Turning the patient on the right side and on the face may help. When the colon has been filled but is relatively contracted, the first radiograms are taken, and the patient is left to rest on the couch for 10 to 15 minutes to allow flocculation to take place.

Second stage: The patient is then instructed to empty the bowel, but not to strain. Two visits to stool may be necessary. When the bowel is empty, there is not a minute to lose, since mucous secretion soon begins to displace the deposited layer. The necessary radiograms should be taken at once, and then the third phase—air-distension—may be undertaken.

Failures in the second stage: (1) There may be no deposition at all. In this case it is best to re-examine at a later date, after thorough preparation, and with a stronger thorium suspension.

(2) Irregular deposition. Flocculation may take place—say, in the right colon and not on the left. In that case it may be feasible to refill the left colon with a stronger suspension, or the partial flocculation may give the desired information. In other cases complete refilling at a later date may be necessary.

(3) Failure to empty: This is likely to occur in elderly subjects, especially in the right colon. Pitressin (5 units) may be effective, but may be too effective, and destroy the pattern. The full $\frac{1}{2}$ c.c. ampoule—10 units—is usually too vigorous in its action.

Prostigmine, 1 to 2 c.c. hypodermically, given twenty minutes before the examination, is recommended by Maingot.

Third stage: inflation of the colon: This is done under fluoroscopic control, a Higginson's syringe being a convenient instrument. Certain difficulties may be met with. The ideal is to fill the whole colon, but often there is some irregularity in the disposition of the gas, and some retained medium. Prone and supine radiograms tend to show these two media in different positions and a composite picture may thus be obtained seriatim.

Radiographic Appearances

First stage: The appearances are similar to those after ordinary barium enema, except that the colon is less distended and the medium less opaque (fig. 6, Plate VI).

Second stage: That of collapse. As the colon contracts its mucosa is plicated (fig. 7, Plate VI). Three types of plicæ are found: haustrations, transverse mucosal plicæ, and longitudinal mucosal plicæ. The two latter are the important ones, and are formed by the action of the muscularis mucosæ. Their form varies with the degree of contraction of the muscular coats, the degree of vascularity of the submucosa, and the secretory activity of the mucous glands.

Longitudinal folds tend to form when the tænia are relaxed, and the gut is lengthened. They are common in the sigmoid.

Transverse plicæ occur when haustra are present. Usually both are present, and from these primary plicæ secondary arborizations frequently arise.

As in the stomach, so in the colon great variation in the normal may occur, and in the present state of our knowledge diagnosis of the pathological should be guarded.

Pathological variations in the plicæ.—Maingot has described the following:—

Plicæ small and numerous: In the so-called irritable colon, a condition which Knothe describes as a reflex disturbance of the neuro-muscular mechanism, e.g. from tuberculous peritonitis, cholecystitis, or chronic appendicitis (fig 9, Plate VII).

Plicæ large and few in number: From any congestion of the mucosa, e.g. catarrhal colitis.

Asterisk or honeycomb pattern: In polyposis; the clear interstices represent the polypi. In diverticulitis a similar star-pattern may radiate from a diverticular neck.

Disorganization of the pattern: In mucous colitis, and more markedly in early ulcerative colitis.

Absence of plicæ: In grave destruction of the mucosa, as in advanced ulcerative colitis, or neoplasm.

Third stage: Three aspects of this should be noted—the colonic calibre, the delineation of its contours, and the appearance of anterior and posterior walls seen *en face* (fig 8, Plate VII).

The calibre when the colon is inflated is 2 to 3 times that of the first stage, and larger than when it is filled with a barium enema. Stenoses are therefore shown, if anything, in greater contrast.

The contour line is of importance, and in the normal there should be a continuous line about a millimetre thick. The French writers call this the "liseré muqueux de sécurité", on the hypothesis that if it is in unbroken continuity it excludes an ulcerative colitis. This "safety line" is by no means infallible: I have seen it present in unbroken continuity in a case of proved active ulcerative colitis of considerable severity. Its absence is of less importance, since that may be due merely to faulty flocculation.

It may be absent in mucous colitis, or broken like morse-code symbols, or again irregular or woolly from excess of mucus. In tumours and ulcerative colitis it is irregular and broken at the site of the lesion, and in diverticulitis it outlines the spiky necks of the diverticula.

The mucosa seen *en face*—i.e. the intermarginal area—is either uniform, when the thin layer casts no shadow, or cracked—like the crazing in pottery-ware—if the layer is too inelastic to withstand the distension. In this intermarginal area various opacities may be seen, such as the rounded shadows of filled diverticula, or irregular blobs of impregnated mucus in mucous colitis. Irregular reticulation may be seen in developed ulcerative colitis with granulomatous proliferations—this is the reverse of the normal crazing, i.e. the reticulum is opaque. Polyposis may produce a negative mosaic, the clear spaces representing the polypi.

Carcinoma shows a complete disorganized irregularity of the intermarginal shadow, constant in serial pictures.

In conclusion, I wish to stress the fact that the thorium-air enema is still to some extent in the experimental stage. Unsatisfactory results, chiefly failure to obtain satisfactory mucous pattern in the collapsed phase, are not a few, but some of these have probably been due to incomplete preparation. Meticulous care in all points of technique may result in a greater percentage of successful examinations.

I think the method has a not unimportant place in the examination of ulcerative colitis (figs. 12, 13, 14, Plate VIII) and of those cases of colonic hæmorrhage and obstruction in which the standard methods of examination have failed to elucidate (figs. 10, Plate VII; fig. 11, Plate VIII).

REFERENCES

- DUVAL, P., and BECLÈRE, H. (1932), *Presse méd.*, **40**, 981.
 ENGEL, A., and LYSHOLM, E. (1934), *Acta radiol.*, **15**, 685.
 HÄRING, W. (1933), *Ergebn. d. med. Strahlenforsch.*, **6**, 407.
 MAINGOT, G., SARASIN, R., and DUCLOS, H. (1935), "Exploration radiologique des colons et de l'appendice au moyen des solutions flocculantes", Paris.
 MYERSON and RITVO (1936), *J.A.M.A.*, **107**, 24.

Dr. R. S. Paterson: *Methods of investigating the large intestine.*—Modifications of old methods and the introduction of new ones have proceeded apace in almost every field of radiological examination. It is curious therefore that with one possible exception, our methods for investigating the large bowel have changed so little since the early days.

PLATE VII



FIG. 8.—Normal thorium-air enema, third stage.



FIG. 9.—Thorium-air enema in a case of mild mucous colitis, showing thickening and increased complexity of the mucosal plicae.



FIG. 10.—Case of sigmoid obstruction from adhesions. Thorium-air enema, first stage. Appearance simulates a carcinoma.

S. COCHRANE SHANKS : Some of the Less Common Lesions and Special Methods of Investigation of the Alimentary Tract and the Influence of Adjacent Organs.

PLATE VIII



FIG. 11.—(Same case as fig. 10.) Thorium-air enema, second stage, showing distorted but intact mucosal pattern in the sigmoid.



FIG. 12.—A case of marked ulcerative sigmoiditis, proved sigmoidoscopically. Barium enema shows no abnormality.



FIG. 13.



FIG. 14.

FIGS. 13 and 14.—(Same case as fig. 12.) Thorium-air enema, first and third stages respectively, showing irregularity of sigmoid contour.

S. COCHRANE SHANKS: Some of the Less Common Lesions and Special Methods of Investigation of the Alimentary Tract and the Influence of Adjacent Organs.

Four procedures are available—the opaque meal, the opaque enema, insufflation with air, and the enema of thorium dioxide. Various combinations of these methods can be employed in special cases. Of these methods the only one that is of recent introduction is the use of colloidal thorium dioxide.

From the technical standpoint the method presents no great difficulty. Nevertheless there are numerous pitfalls, and even its most enthusiastic users agree that the interpretation of the findings still requires further work before they be accepted as indisputable. The degree and nature of the flocculation may give rise to false appearances and it is difficult to be assured that the deposit on the mucosal folds is sufficiently even and complete to give an accurate picture of their pattern. Thorium dioxide can in no way be considered as a substitute for the barium enema, at any rate in the present state of our knowledge, but there is little doubt that in selected cases it will be a valuable adjunct.

I have interpreted the title of this discussion as meaning that carcinoma, diverticulitis and megacolon must be excluded from it. Of the remaining lesions I propose to confine myself in the short time available to the following:—

- (1) Anatomical variations. (2) Intussusception. (3) Colitis: (a) simple, (b) ulcerative. (4) Polyposis. (5) Tuberculosis.

My comments on these must be brief and far from exhaustive, but I have a few cases to illustrate each of the conditions which may be of interest.

Anatomical variations.—I mention these chiefly for the sake of completeness. They were dealt with very fully at a recent meeting by Dr. Shanks. Apart from redundant loops, the two commonest variations are due to failure to descend and failure to rotate—giving rise to the so-called undescended caecum or hepatic caecum in the one case and to right-sided ascending colon or caecum in the other. Faulty fixation by excessively long mesentery may be responsible for hypermobility of various sections of the large bowel.

Intussusception.—This condition may occur in both children and adults—in the latter it is more commonly associated with a polyp or a small growth.

The chief radiological signs are:—

- (1) The arrest of the enema at the head of the intussusception.
- (2) The gradual tailing off of the Ba shadow and its division as it flows between the two layers of the invaginated bowel.
- (3) Sometimes there may be a thin streak of barium in the lumen of the intussusception.

A number of cases are on record in which the giving of an opaque enema had reduced the intussusception producing a spontaneous cure.

I am indebted to Dr. Courtney Gage for the following report:—

The patient, a girl aged 6 years 1 month, had a severe attack of abdominal pain associated with diarrhoea and the passage of blood and mucus. On examination *per rectum* a tender mass was felt and seemed to be attached by a pedicle.

The patient was admitted to hospital. On further examination no tumour could be felt *per rectum* and examination by barium enema was undertaken.

The enema flowed into the left half of the transverse colon and then became suddenly arrested. After an interval of ten minutes screen examination showed the typical appearance of an intussusception. No fluid passed beyond the hepatic flexure but some reduction of the intussusception took place. Operation showed an intussusception with a large fibroma at the apex of the intussusception.

In comparison with this I will describe the films from a case which I saw quite recently.

The patient, a woman aged 60, had been admitted to a nursing-home with symptoms of subacute obstruction and a history of several previous less severe attacks. She appeared ill and had lost weight. The acute symptoms subsided after enemata had been given and the

patient was referred for X-ray examination. There was a palpable hard mass in the right iliac fossa and a provisional diagnosis of carcinoma of the cæcum had been made.

An opaque enema flowed without interruption round to the cæcum, where it was arrested, showing a smooth convex margin. The palpable mass was obviously involving the cæcum and could be moved with it. The curious features of the case were the smooth convex upper border and the extreme hardness of the palpable mass. I came to the conclusion that this was a small cæcal carcinoma which had become intussuscepted.

At operation there was found a large fæcalith, stony-hard, impacted in the lower pole of the cæcum and blocking the ileo-cæcal valve; there were no signs of malignancy. The mass was removed with difficulty, owing to its size and hardness. The patient made an uninterrupted recovery.

It is, of course, easy to be wise after the event. I think I was misled by the clinical history and did not give enough weight to the lack of deformity of the cæcum, its mobility, and the hardness of the mass: but it must be admitted that the appearances are very like those of intussusception and that fæcaliths in this situation are extremely rare. I think a "double contrast" enema might have revealed the true state of affairs.

(3) *Simple colitis*—which I take to mean an infection of the colon with inflammatory changes, chiefly involving the mucosa and submucosa—may be either acute or chronic. In the acute stage, when severe, it may be impossible for the patient to retain an enema at all. The bowel is in a state of acute irritability and active spasm. The radiological appearances are very much those of a spastic colon from any other cause. The lumen is much narrowed and the normal appearance is replaced by a thin line of barium—no thicker than a pencil. Personally I find great difficulty, on purely radiological appearances, in making a differential diagnosis between a spastic colon and a simple colitis. This is one of the cases in which an enema of thorium dioxide may be of service. There must be changes present in the pattern of the thickened and inflamed mucosal folds in colitis, and if accurate pictures of these can be obtained, they should be characteristic. Sarasin has recently shown this to be the case, with a series of mucous-membrane pictures showing a blurred and tufted appearance of the pattern, which he regards as recognizable and associated with a condition of colitis.

In the more chronic forms of colitis the spasticity becomes less marked and the acute irritability subsides. The enema is usually administered without difficulty and occasionally there may be wide dilatation of the lumen. Often the enema flows very rapidly—at any rate as far as the splenic flexure. The shadow of the colon is parallel-walled and there is a marked diminution, or complete absence, of the haustral markings—the so-called "ribbon" colon. These appearances may also be found in ulcerative colitis and a radiological differential diagnosis is far from certain. "Notching" of the shadow has been described as representing ulcer craters but this is, in my experience, an unusual finding.

The most likely way of showing the actual ulcers is by means of the thorium enema or the double contrast method, by which it is quite possible to demonstrate the ulceration.

The diagnosis of colitis is really a clinical one and though I do not minimize the value of the assistance of a radiological examination, its greatest value is in assessing the extent and severity of the condition rather than in showing its presence.

(4) *Polyps* may occur anywhere in the large bowels—they may be relatively large and single or the whole mucosa may degenerate into a mass of multiple small polyps. The large single polyps usually show clearly as a filling defect in the barium shadow and when seen do not present any great difficulty in diagnosis. There may be several present in the course of the bowel. Polyposis when extensive gives rise to a very characteristic appearance. There is a mottled or marbled effect on the shadow, produced by the multiple areas of lessened density caused by the polyps. It can be most beautifully shown by the double contrast method, using either barium

or diagenothorine. The pitfall in these cases comes from faecal retention. Certain foods seem to give rise to a mottling of the faecal shadow, which may be indistinguishable from that in polyposis, and in pancreatitis the large quantity of fat in the faeces may give rise to an appearance almost identical. The remedy is obvious. These cases should have particular attention paid to their preparation, and radiograms should be taken with the enema in situ and after evacuation, respectively. A comparison of the two films will show whether there has been any shift of the shadows.

A final point about polyposis which I may mention is that in long-standing cases the polyps are liable to undergo malignant degeneration, and a look-out should be kept for irregularities which may indicate that this has occurred. In these cases also the double contrast method is particularly valuable.

(5) *Tuberculosis*.—I included tuberculosis of the large bowel as the last of the less common lesions. The subject is much too large to be dealt with in a paper of this nature.

The ileo-caecal region is by far the commonest site of tuberculous infection, and the most difficult differential diagnosis is from malignancy of the same region. The chief signs are a gross irregularity of the outline, often extending to the ascending colon and terminal ileum, tenderness, and a palpable mass.

Stierlin's sign, though not pathognomonic, is always present. It consists in a rapid emptying of the caecum and ascending colon the moment the pressure of the enema is released. More recently Sarasin has described a funnel-shaped deformity, seen with a double contrast thorium enema, which he thinks is characteristic.

Dr. G. Bush: *The influence of adjacent organs and tumours on the alimentary tract*.—Displacements of portions of the digestive tract may be due to a variety of causes. They naturally group themselves into congenital and acquired displacements, and I propose briefly to consider some of the acquired displacements due to extrinsic causes, such as tumours and enlargements of adjacent organs. Time also limits me to a consideration of such conditions below the diaphragm.

When an abdominal tumour can be felt, doubt often arises as to its nature, size, site of origin, and so forth; it is when clinical signs and symptoms are not conclusive that an investigation of the alimentary tract by means of an opaque meal, or enema, or both, may often yield valuable information to the physician or surgeon in planning treatment.

Sometimes a routine alimentary investigation will reveal a displacement that leads to the discovery of an unsuspected mass or visceral enlargement. This may occur in very obese patients, or when the tumour or enlargement is situated in a region where palpation is difficult, such as under the left costal margin, or deep in the pelvis. For example, a moderate enlargement of the spleen may escape clinical detection, but is at once obvious to the observant radiologist, who notices a displacement of the stomach to the right and of the splenic flexure downwards, together with an outline of the enlarged organ demonstrable in good radiographs.

Before proceeding to detail I will enunciate a few general principles.

In conducting such an investigation the examiner must have a full appreciation of the wide normal variations in the position and shape of the different sections of the digestive tract in persons of different habitus and under the influence of posture. He must also have a knowledge of the anatomy of the peritoneum and its mesenteric folds, and appreciate the general shape of the abdominal cavity, with its hollows and recesses, as these are important factors in determining the range of mobility of the viscera and their possible response to the influence of outside pressure. A combination of a displacement of part of the gut with a restriction of normal mobility, demonstrated by careful radioscopic palpation, is of more value in arriving at a conclusion than the demonstration of either of these alone.

I will now show some examples of such displacements affecting different parts of

the tract. In many of them the effect will be quite obvious but we all get surprises periodically, and some, I hope, will be of special interest and illustrate some important anatomical and diagnostic points.

For the loan of some of the slides from which these diagrams were constructed I am greatly indebted to Dr. Courtney Gage.

EXAMPLES OF DISPLACEMENTS

An enlargement of the spleen will compress and displace the stomach to the right and somewhat forwards (fig. 1). The indentation on the greater curvature may simulate the appearance due to a carcinoma of this curvature (fig. 2). I need not waste time on the methods of differentiating the two, but these two slides illustrate well how misleading radiographs alone may be in alimentary examinations.

Enlargements of the spleen also depress the splenic flexure of the colon (fig. 3). The colico-splenic ligament normally anchors the splenic flexure firmly to the hilum of the spleen, so that any downward displacement of this flexure is generally pathological. The patient was a fat woman with a palpable tumour in the left hypochondrium, thought to be renal. Barium examinations showed the stomach displaced to the right and the splenic flexure downwards. Pyelography showed the left kidney to be slightly depressed, but normal in size and function.

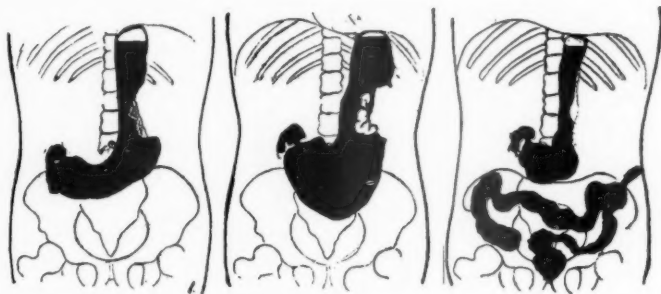


FIG. 1.

FIG. 2.

FIG. 3.

The effect of left renal tumours or enlargements on the stomach is variable, depending on the type of the stomach and the volume of its contents, and of course on the size of the renal enlargement and whether the whole kidney is involved or only the lower pole, as in some cases of hypernephroma. Fig. 4 is from a case of a large renal tumour displacing the lower half of the stomach downwards and to the left, indenting the lesser curvature.

The splenic flexure is not usually affected, but the descending colon will be displaced forwards and sometimes towards the mid-line.

Fig. 5 is from a case of a large left renal tumour displacing the stomach upwards, and the descending colon forwards and inwards. Notice that the splenic flexure is still anchored up to the spleen. Retroperitoneal sarcomata may produce a variety of effects depending on their size and position (figs. 6 and 7). Here is one displacing the pyloric portion of the stomach upwards and the small intestine and the transverse colon downwards, but the fixed part of the duodenum is not definitely affected.

In contrast with those, enlargements of the head of the pancreas splay the duodenum outwards into a wider circle than normal (figs. 8, 9, and 10). These pancreatic enlargements are more commonly cysts, but may be due to carcinoma.

There is nothing special to say about the effect of enlargements of the liver (fig. 11, from a case of hydatid enlargement) as the displacements of the stomach and colon are unmistakable, but I would remind you of the frequent occurrence of a Riedel's lobe and its effect on the adjacent portion of the colon.

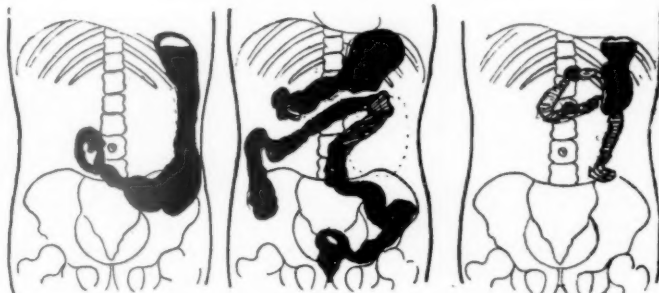


FIG. 4.

FIG. 5.

FIG. 6.

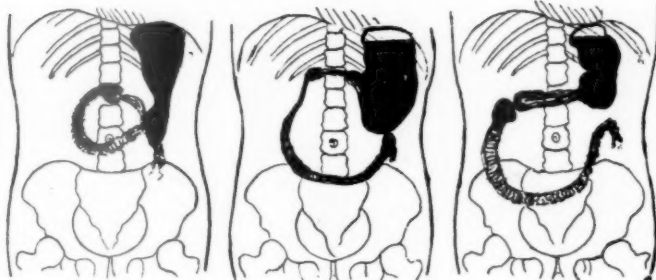


FIG. 7.

FIG. 8.

FIG. 9.

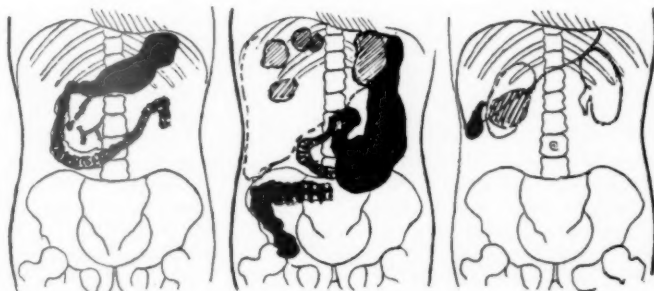


FIG. 10

FIG. 11.

FIG. 12.

Less common, perhaps, is a displacement of the gall-bladder (fig. 12). The patient had biliary symptoms, with a palpable tumour in the site of the gall-bladder, thought to be an enlargement of this viscus. Cholecystography revealed the gall-bladder displaced laterally, and at operation a simple cyst of the liver was found where the gall-bladder should have been.

With regard to the colon, many tumours in the upper abdomen will affect the position and mobility of the transverse colon and the two flexures, and their effect on the colon should be studied, in addition to that on the stomach and duodenum, if all available information is to be obtained.

In tumours and swellings found below the level of the umbilicus an examination of the colon by means of an opaque enema is generally sufficient, although at about four hours after an opaque meal an upward displacement of the terminal coils of the ileum will often be found where there is a right-sided or central pelvic swelling. Turning to the influence of pelvic swellings on the sigmoid, I have found the examination of these cases most interesting and instructive. The proximal two-thirds or so of the sigmoid, being one of the most mobile parts of the colon—owing to its possession, usually, of a complete and often somewhat lengthy mesentery—can readily suffer displacement by pelvic masses.

One must be quite sure, however, that a true displacement is present, by demonstrating a reduction in its mobility by careful radioscopic palpation and posturing, bearing also in mind the possibility of a redundancy of the sigmoid simulating a displacement due to extraneous pressure (fig. 13).

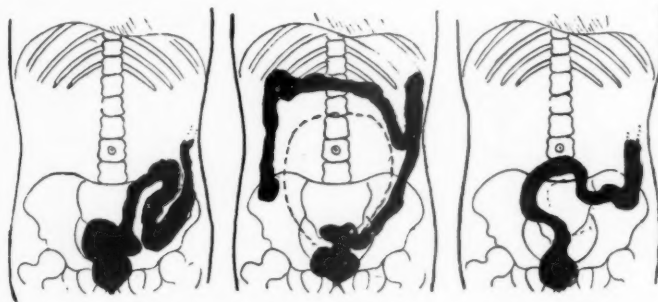


FIG. 13.

FIG. 14.

FIG. 15.

A moderate enlargement of the uterus has little effect on the sigmoid beyond a slight displacement to the left. Even a uterus at about the sixth month of pregnancy (fig. 14) only depresses the sigmoid downwards somewhat. Its effect on the transverse colon is much more marked. The explanation of these effects in the pelvis is a simple anatomical one, namely that the uterus enlarges, at first, along the axis of the pelvic inlet, and this axis is nearly at right angles to the plane in which we usually visualize the abdominal portion of the colon. One is very liable to forget this point when looking at antero-posterior radiographs. Frequent visits to the post-mortem room will correct the radiologist's tendency to a two-dimensional outlook.

I have not had enough opportunities of examining the colons of women with uterine fibroids to say anything about their effect in this connexion, or to draw any definite conclusions about the value of an examination of the sigmoid in the differential diagnosis of these tumours, but I have found a fairly constant type of displacement in cases of simple or malignant ovarian cysts of moderate dimensions. I should be glad to hear of other members' experiences in cases of fibroids.

Here is a figure from one of three cases of ovarian cyst (fig. 15) which shows the sigmoid pushed upwards and the S-bend uncurled into an inverted "U". In four of these cases the patients had a palpable tumour in the pelvis; in two it was just palpable, and in one barely palpable through the abdominal wall. In all, the normal mobility of the sigmoid was found to be restricted.

The next case was an interesting contrast with the three previous ones. It was that of a woman with a hardish, ill-defined swelling behind the pubes, rather to the left of the mid-line. On the filling of the colon with an opaque enema, the distal part of the sigmoid was displaced to the right while the proximal loop was somewhat compressed but not pushed upwards (fig. 16). On rotating the patient on to her left side, the proximal loop appeared to move up out of the pelvis (fig. 17) and filled well. It seemed to me that the most likely cause of this combination of a displacement, without a restriction of mobility, was a fluid swelling, such as an abscess, and this proved to be the case, for at operation a pyosalpinx and pelvic abscess were found. This case illustrates the importance of the two criteria I laid down at the beginning, namely displacement *plus* restriction of mobility.

Tumours in the pelvis occasionally cause obstruction in the sigmoid by direct pressure against the pelvic brim, but usually the sigmoid is sufficiently mobile, on account of its long mesentery, to adapt itself and avoid this complication.

The next case was sent for investigation, having symptoms of subacute obstruction in the lower bowel and a palpable tumour. I found a partial obstruction in the lower end of the descending colon, opposite the pelvic brim, the sigmoid being displaced slightly downwards and showing a restriction of mobility. A radiograph

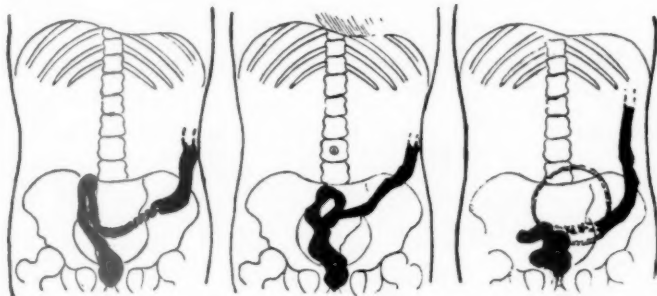


FIG. 16.

FIG. 17.

FIG. 18.

showed the outline of a largish thick-walled cyst (fig. 18), which, at operation, was found to be a dermoid attached to the posterior wall of the pelvis. Owing to its site of origin, the tumour, as it enlarged, pushed the sigmoid downwards into the pelvis, so that it could not escape as in the case of an ovarian tumour which would arise below it.

The last two figures illustrate two rather remarkable cases. The first, referred to me by Dr. Hall of Burnham, was in a woman who had a very large abdominal tumour occupying mainly the upper half of the abdomen. I found a gross displacement of the stomach and small intestine to the right, and of the transverse and splenic portions of the colon downwards, by an enormous mass which later proved to be an intra-abdominal lipoma originating right up under the left dome of the diaphragm (fig. 19). This demonstration of the size and extent of the tumour forewarned the surgeon that an operation for its removal was likely to be a laborious and difficult one, but, nothing daunted, he removed the majority of it successfully. It was as large as a football, and it weighed 7.6 pounds. After a stormy passage the patient recovered, and is now back at work.

The second was an example of a secondary complication that may occur from the contiguity of an abdominal tumour to an adjacent part of the alimentary tract. It was in a woman with a large lower abdominal swelling and tympanites. Apart from the visceral displacements caused by the tumour, I found that the tumour itself was

distended with gas like a balloon (fig. 20). It was an ovarian cyst which had become adherent to the sigmoid. A small fistulous connexion between the sigmoid and the cyst had occurred, owing, as far as could be discovered at operation, to an inflamed diverticulum in the sigmoid. The cyst had become infected with gas-forming organisms and the balloon-like tumour shown was the result. The cyst, when opened, was found to contain foul-smelling gas and only a little purulent fluid. Unfortunately the patient was too ill to recover and succumbed a few days after the operation.

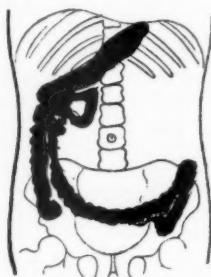


FIG. 19.

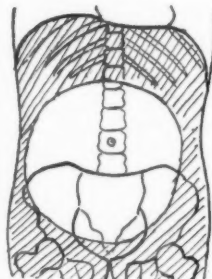


FIG. 20.

In conclusion, I hope I have been able to show that a careful X-ray examination may add useful information to that obtainable by clinical investigation and other laboratory methods, in cases presenting abdominal tumours, and that such information, always interpreted in the light of the clinical history and findings, is well worth obtaining and putting at the disposal of the responsible medical attendant or surgeon, for the benefit of the patient.

I wish to record my thanks to those colleagues who have referred many of these cases to me for investigation, and to Dr. Courtney Gage and Dr. Cochrane Shanks for the loan of some of the figures from which the diagrams were constructed.

Section of Laryngology

President—LIONEL COLLEDGE, F.R.C.S.

[May 7, 1937]

Multiple Metastasizing Melanomata.—NORMAN PATTERSON.

W. S., aged 38, male.

13.4.37: Five weeks ago noticed several small dark nodules on left side of neck. Three weeks ago noticed that urine was dark. Two weeks ago noticed many small nodules over the body and limbs. Sight good. Occasional attacks of vomiting. No hæmatemesis or melæna.

On examination.—There are pigmented areas in the mouth, pharynx, and larynx, small dark areas on the posterior third of the tongue, a large patch on the epiglottis, and numerous patches on the arytenoids and aryteno-epiglottic folds. The nasopharynx appears to be clear of pigmentation. There are also bilateral nasal polypi. The trachea, bronchi, and œsophagus have not been examined.

Identification of pigment from urine: Melanin.

Blood-count: Hæmoglobin = 102%; colour-index = 0.98.

Microscopical diagnosis.—Two nodules of very pigmented secondary spindle- and polygonal-celled melanotic carcinoma in subcutis of arm.

Carcinoma of Tongue, followed by Cystic Adenoma of Thyroid.—

NORMAN PATTERSON.

E. P., female, aged 67.

8.8.32: Infiltrating carcinomatous tumour of right side of base of tongue and lower pole of tonsil. No enlarged glands in neck.

10.8.32: Local excision of growth by diathermy.

12.8.32: External carotid ligatured, owing to hæmorrhage in bed of wound.

5.2.37: Presented herself with swelling in the right side of the neck, deep to the sternomastoid. The swelling was firm, appeared to be attached to the deep structures, and did not move on swallowing; its surface was somewhat nodular. It was thought to be a recurrence in the glands of the neck, but when the patient was operated on, 17.2.37, the tumour was found to be associated with the thyroid gland, and was easily removed.

Histological report.—"Fibrous-walled cyst and a calcareous nodule surrounded by fibrosis apparently from a nodular colloid goitre. Variability in shape and size of vesicles, epithelium frequently cubical; moderate fibrosis and focal lymphocytic infiltration in surrounding thyroid tissue."

Subsequent course satisfactory. No signs of any growth at site of original carcinoma.

Laryngectomy for Carcinoma of Larynx, with Development of Secondary Gland nearly Five Years after Original Operation.—NORMAN PATTERSON.

F. D., male, aged 66.

7.8.32: Anterior portion of right cord, anterior commissure, anterior two-thirds of left cord, and inferior laryngeal surface of epiglottis were involved. Left cord fixed. No glands palpable in neck.

10.8.32: Laryngectomy performed, including removal of the epiglottis, and upper two tracheal rings. Recovery uneventful.

Histological report.—Squamous, polygonal- and trabecular-celled carcinoma of larynx.

7.4.37: For two months has noticed lump, gradually increasing in size, on left side of neck.

On examination.—Large, firm and very adherent swelling, lower part of neck deep to sternomastoid. No other glands palpable.

14.4.37: The swelling was removed by a dissection which included removal of a section of the sternomastoid and the underlying and adherent jugular vein, which was divided just above the entrance of the thoracic duct, well below the tumour, and again above the tumour, about half-way up the neck. On examination of the specimen the outer wall of the vein was seen to be invaded. No other enlarged glands could be palpated.

Histological report.—Squamous- and prickle-celled trabecular secondary carcinoma of neck, replacing lymphatic gland.

The Evidence of Comparative Anatomy on the Structure of the Human Larynx

By V. E. NEGUS

THE human larynx has undergone many changes in the course of evolution, and is now a complicated organ. It is possible, however, to study its component parts in the light of comparative anatomy and thus to derive information as to the reasons for the various structural details.

The position of the larynx, low in the neck, is one peculiar to man; there is a gradual descent from infancy to adult life. Changes in the pituitary and occipito-vertebral angles have an influence, but not one of supreme importance. A similar position of the head in relation to the vertebral column is present in the higher apes, without a corresponding alteration in the level at which the larynx is placed.

The factor of greatest importance is recession of the jaws, with consequent backward and downward displacement of the tongue. As the larynx must necessarily lie behind the tongue, it is forced to occupy a lower position in man than in a gorilla, for instance, in which there is a protruding snout.

In reptiles, birds, and most mammals, the head is in line with the axis of the vertebral column and the mouth is projecting; in such animals the larynx lies opposite the base of the skull. One consequence of the low position of the larynx in man is the formation of a capacious pharynx, of great value for phonation.

The size of the larynx in man is small in relation to his body-weight. It is also small in proportion to the size of the trachea, thus producing a choked point on the airway, with less facility for rapid exchanges of gases in the lungs, than in more active species. Owing to his greater intelligence, man does not require the strength or speed of animals and does not suffer from his narrow airway in the struggle for existence.

In the foetus and the child the larynx is relatively bigger, if compared with the trachea; it is somewhat-funnel shaped and resembles, in this respect, the larynx of the dog tribe, amongst other animals. It is also larger in the male after puberty, than in the boy or female.

The laryngeal aperture, in relation to the axis of the pharynx, is not at a right angle, as in reptiles and birds, and not in line with the trachea, as in fast-running deer and many other animals; it is set obliquely. Consequently there is friction as air passes to the lungs. In the process of development from embryo to foetus there is a gradual tilting of the laryngeal aperture, until in the adult it is inclined towards the opening of the nasopharynx.

The scaffolding consists of thyroid and cricoid cartilages, the one movable on the other, with consequent advantages in deglutition and phonation. There is added facility in opening and closing the laryngeal aperture, because the margins of the glottis are made up of short arytenoid cartilages and long membranous folds.

In reptiles and birds there is a single crico-thyroid plate, while in marsupials the thyroid and cricoid cartilages are fused. In both types the arytenoids are long,

and closure of the laryngeal aperture is attained mainly by lateral coaptation of the cartilaginous margins, rather than by forward movement of the arytenoids, as in man.

The *extrinsic muscles* cause the larynx to move during deglutition and phonation, and to partake in the peristaltic wave executed by the pharyngeal muscles. In such animals as the chameleon the pharynx is capacious and the larynx very small; it is easy to learn from this species that the larynx merely partakes in the movements of the pharynx. In man the larynx is large in relation to the pharynx and thus the primitive mechanism is obscured.

The *epiglottis* of man is almost functionless. It is not in apposition with the soft palate, as in most animals, in which it serves as an accessory organ of olfaction. In man the olfactory sense is not of importance and it is not of vital significance if the inspiratory air current enters by the mouth. In such animals as herbivora, such an occurrence would be dangerous to life, as the sense of smell would be diminished when the mouth was open. In an animal such as the horse there is a powerful hyo-glosso-epiglottic muscle to move the large epiglottis, but in man there is merely a ligamentous relic in the position of these contractile fibres.

The *arytenoid cartilages* of man are short, because of the relatively slight necessities of respiration; the membranous folds are long in proportion. The larynx itself is relatively small, and the two factors combined produce a choked point on the airway. In some fast-running animals the larynx is large and forms a funnel-shaped dilatation at the upper end of the trachea, whilst in others the arytenoids are long and produce wide dilatation of the glottis. The derivation of the arytenoids from lateral cartilages can be studied in the embryo and can be compared with the adult form of some amphibians. The presence of rigid bars in the glottic margins is of assistance in opening the glottis during respiration.

The *intrinsic muscles* are divided into a sphincteric and a dilator group. Comparison with the muscular sphincter of the Dipnoi or lung-fish, amphibians, reptiles and birds, allows an understanding of the division of the sphincter into separate muscles to be obtained. It is easy to see how the lateral crico-arytenoid, thyro-arytenoid and inter-arytenoid muscles are all parts of a sphincteric girdle, and have a synergic action in deglutition and phonation. Many fibres run from one muscle into another.

The dilator group of man is represented by the posterior crico-arytenoid muscles, which work in opposition to the sphincteric group. They do not pull on the tips of the arytenoid cartilages, as in reptiles and birds—thus causing the glottis to assume a triangular shape, with the apex placed posteriorly—but are attached to the muscular processes and work in two ways. They rotate the glottic processes of the arytenoids outwards, but there is also a second action, not usually recognized, namely separation of the bodies of the arytenoids by the pull of lateral fibres of the muscles. This movement is made possible by the laxity of the crico-arytenoid joints, and is not seen in lower animals. The result of the combined actions is that the glottis, when open during respiration, assumes the shape of a triangle with the apex placed anteriorly.

The *cartilages of Santorini* are backwardly curved, to give partial attachment to the anterior wall of the œsophagus. The object of this attachment is made clear by comparison with certain animals, as for instance, herbivora. When the larynx closes during deglutition the crico-pharyngeal sphincter relaxes and the mouth of the œsophagus is pulled open by its attachment to the cartilages of Santorini, so as to assume a funnel shape. In man there is, in addition, partial attachment of the œsophagus to the back of the cricoid cartilage, so that the mechanism described is not of great importance.

The *laryngeal ventricle* divides the primitive thyro-arytenoid fold into two divisions—upper or ventricular band, and lower, or vocal cord. It has no vocal function, but is merely a recess left by separation of the two folds; this is well

illustrated by comparison with the Japanese deer (*Cervus sika*) and other animals, in some of which there is merely a shelf-like depression between the inner and outer divisions of the thyro-arytenoid muscle.

The vocal cords of man have margins of a moderate degree of sharpness; they act as a valve of considerable efficiency—inferior, however, in respect of prevention of air entry, to the similar structures of lemurs, monkeys, and apes. The valve is required in animals which climb, and in man it shows signs of retrogression. The result is an improvement in respect of phonation, as a wider range of tones can be executed by the human vocal cords than by the sharp-edged folds of apes, for instance. The tones, also, are more mellow. Short cartilages and long folds are essential if a wide range of sound is to be produced. In reptiles or birds the long arytenoid cartilages preclude efficient phonation at the larynx. In birds the vocal necessities are supplied by the provision of a syrinx at the bifurcation of the trachea.

The ventricular bands are free-edged and valvular and are capable of retaining air in the lungs at times when straining is called for to raise the intra-abdominal pressure. Very few animals have folds of a similar valvular nature, the probable reason being the lesser degree of mobility of their ribs.

The sacculi are small and insignificant, as compared with that of some apes. In man it seldom reaches above the upper margin of the thyroid cartilage, but in chimpanzees it is continuous with air sacs which extend into the axilla for purposes connected with the rebreathing of air.

The aryteno-epiglottic folds form the mesial boundary of the lateral food-channels, along which liquids may pass, even when the laryngeal aperture is open. In man the folds are neither high nor efficient, but in infants the channel is relatively better formed and permits of simultaneous deglutition and respiration. The lateral channel is seen to advantage in the cetaceans and herbivora, in which large quantities of liquid or semi-liquid food has to pass into the oesophagus.

The cartilages of Wrisberg support the aryteno-epiglottic folds and are tall and slender; they help to fill in the gap between the epiglottic and arytenoid cartilages.

CONCLUSIONS.

For protection of the lungs the larynx of man is efficient. There is a sphincteric muscle-girdle to close the laryngeal aperture and there are also upstanding ary-epiglottic folds to provide lateral food-channels and thus prevent inundation by liquid while the aperture is open.

For combined respiration and deglutition, efficiency is slight in the adult but better in the infant. The powers of olfaction are slight in man, as reflected in the inefficiency of his epiglottis and its lack of apposition to the soft palate.

Respiration is not served to the degree of efficiency seen in many animals. The larynx of man is always a choked point on the airway, whenever the needs of respiration are considerable. The airway is tortuous and provides various points of friction, thus providing yet another check to the efficiency of gaseous exchanges in the lungs.

There is no mechanism for respiration at times when no fresh air is entering by the nose and mouth, as there is in some mammals, certain reptiles, and most birds.

Phonation is well served by flexible and long vocal cords, capable of varied degrees of elasticity. The presence of a capacious pharynx, owing to the low position of the larynx, gives man considerable advantages. His powers of speech are greatly assisted by the lack of contact between the larynx and the soft palate and the consequent ability to emit sounds both by mouth and nose.

When all the structural details are considered the conclusion is that the larynx of man is not specialized for any one function, but is an extremely versatile and efficient organ.

Section of Laryngology and Section of Otology

COMBINED MEETING

HELD AT NORWICH, JUNE 18 and 19, 1937

LARYNGOLOGICAL SESSION

(Chairman: LIONEL COLLEDGE, F.R.C.S. (President of the Section of Laryngology))

DISCUSSION ON ORBITAL CELLULITIS DUE TO SINUS INFECTION, AND ITS TREATMENT

E. D. D. Davis: Orbital cellulitis is an acute inflammation of all, or a part, of the contents of the orbit, characterized by œdema of the eyelids and conjunctiva. When the inflammation progresses to suppuration the œdema rapidly increases, the eyeball becomes immobile and displaced forwards, and the conjunctiva becomes so œdematous as to protrude between the eyelids. Nasal sinusitis complicated by simple œdema of the upper eyelid, which disappears with conservative treatment, is not considered to be orbital cellulitis. Owing to the rigidity of the walls of the orbit, the tension and compression are severe, and contribute to the thrombosis of blood-vessels and injury to the contents of the orbit. This compression of the veins may account for some of the œdema of the eyelids. The three fascial compartments formed by the orbital periosteum and the capsule of Tenon add to this tension, hence the pain and compression arising from hæmorrhage into the orbit. Wolff has described these fascial compartments in detail, and has shown that pus may be found firstly, between the orbital periosteum and the bone; secondly, between the orbital periosteum and the capsule of Tenon which contains the orbital fat, vessels and nerves—a truly dangerous area; and thirdly—the more rare position—between the capsule of Tenon and the globe of the eye. Orbital cellulitis is always a serious and dangerous condition and has sometimes terminated in cavernous sinus thrombosis, meningitis, brain abscess, septicæmia, and optic atrophy.

There are three paths by which inflammation can extend to the orbit. The first, and commonest, is a direct spread from the nose through the bone or along the ethmoidal vessels. The second is by the blood-stream when the orbital cellulitis is part of a septicæmia or pyæmia. I have only seen one such case—a panophthalmitis due to embolism from a lateral sinus thrombosis. Osteomyelitis of the orbital bones, especially of the infra-orbital margin and maxilla, is seen in infants, on rare occasions. The third way is by lymphatic spread, but it is doubtful if it ever occurs. There are a few lymphatic vessels, but there are no glands in the orbit. These lymphatics drain into the parotid and deep cervical lymphatic nodes and do not extend to the nose.

I have the notes of 54 cases of œdema or swelling of the orbital contents, which have been sent by ophthalmic surgeons for examination of the nose, with the following diagnoses:—

Frontal sinus suppuration	24
Ethmoidal sinus suppuration	15
Injury	4
Orbital tumour	5
Optic nerve tumour	2
Foreign body and abscess	1
Suppurating cyst	1
Metastatic panophthalmitis	1
Syphilis	1
		54

It will be seen that 39 of the cases arose from nasal sinus suppuration, that is 72%. Six cases of cavernous sinus thrombosis have not been included in this list.

In my experience the commonest cause of inflammation of the orbit of nasal origin is suppuration of the frontal sinus in adults, and ethmoidal suppuration in children. I have not seen any cases of antral or sphenoidal suppuration extending to the orbit. Extension from the antrum to the orbit, in the adult, is usually due to a new growth. The pus from the frontal sinus bursts through the thin bony floor of the frontal sinus, just to the inner side of the supra-orbital notch, and an orbital abscess is formed between the bone and the orbital periosteum. Similarly, pus from the ethmoidal cells tracks through the thin os planum or inner wall of the orbit, usually near the posterior edge of the lacrimal bone. In a few cases the pus is near the foramen of the anterior ethmoidal artery. The abscess in both cases is like a collar-stud, a collection of pus lies between the bone and the orbital periosteum, and a second collection is situated in the affected nasal sinus. It is essential to drain both collections of pus, and particularly that of the nasal sinus. It is also important to respect and avoid injury to the orbital periosteum which forms an effective barrier between the abscess and the delicate orbital contents. In some cases, œdema only of the orbital tissues occurs, without abscess formation, and in such a case, drainage of the causative nasal sinus by an intranasal operation alone is sufficient and results in a disappearance of the œdema.

Frontal sinus suppuration produces a characteristic downward and outward displacement of the eyeball, and the maximum swelling is over the floor of the frontal sinus and at the inner third of the supra-orbital ridge. Ethmoidal suppuration displaces the eyeball outwards. This displacement of the eyeball is almost diagnostic of sinus suppuration which has extended to the orbit. Examination of the nose in the great majority of cases reveals signs of sinus suppuration, and pressure on the external swelling may cause pus to exude into the nose. On the other hand, a mucocele which is a closed distension of a nasal sinus, resembles a tumour; it may show no signs of inflammation, and the nose is frequently normal.

When the œdema of the orbit is great the more serious condition of cavernous sinus thrombosis is feared. In the early stage of thrombosis, the differential diagnosis may be difficult, but a patient with cavernous sinus thrombosis is desperately ill with frequent rigors, and the œdema is soft and has a bluish tint which extends to the other eye and face. Œdema near the mastoid emissary vein is sometimes present. Diplopia and paresis of an ocular muscle are early signs. The pupil is dilated and inactive; blindness is rapid in onset and—most important—a primary source of infection, such as a boil of the face, or middle-ear suppuration, is present.

A brief reference should be made to the four cases of injury resulting in hæmorrhage into the orbit, which was followed by suppuration. Three of these were due to direct blows. In one case the roof of the orbit was fractured and three weeks later a frontal lobe abscess and meningitis were found, terminating in death. The fourth case of injury was one in which cellulitis developed after a vigorous nasal operation for extensive ethmoidal disease with perforation of the orbital wall.

Tumours of the orbit, or of the optic nerve, have been mistaken for an orbital abscess, especially when nasal sinus suppuration and a tumour existed together, or rather, when the condition of the nose suggest sinus disease. I have seen one case of a tumour of the optic nerve in which the sphenoid and posterior ethmoidal sinuses were explored because the nose was not above suspicion, but with a negative result. The differential diagnosis is made in these cases by a process of exclusion.

Œdema of the upper eyelid, as a result of a septic infection of the scalp, is well known and characteristic.

The treatment of an orbital abscess arising from the nose is always urgent, and more urgent than that of an acute mastoid. The indications of an orbital abscess are an increasing and brawny œdema of the eyelids and conjunctiva, a fixed and displaced eyeball, and excessive pain. Pressure on the swelling of the orbit may cause pus to

exude into the nose. When an abscess is present there should be no hesitation in establishing adequate drainage. The cornea must be protected from abrasions; when the patient is being anesthetized, castor oil is dropped into the eye, and before making the incision the eye is closed by a stitch passed through the loose skin of the eyelids. At the end of the operation the stitch is removed and there is no subsequent stitch scar; this is important, because perforating ulcers of the cornea have occurred from septic abrasions. The pressure of a tight eye-bandage may also cause an ulcer of the cornea. An incision is made along the inner two-thirds of the supra-orbital ridge in the line of the eyebrow, and carried down below the inner canthus. The incision must be long enough to obtain a good access to the site of the abscess. With the complete arrest of hemorrhage, gentle retraction, and a little dissection, the origin of the abscess can be easily inspected. The stab incision and thrust of sinus forceps is insufficient and uncertain. It often fails to find pus, is usually made too low in the eyelid, and may perforate that important barrier and protector of the orbital contents, the orbital periosteum, and so spread infection.

In some cases the oedema of the orbit has been slight and confined to the upper eyelid, and no suppuration within the orbit has been present. A number of such cases have been recorded, in which conservative treatment has been sufficient. During the early acute stage, before suppuration is present, conservative treatment is advisable. Children with sinusitis are more susceptible to oedema of the orbital contents, and most of the successful cases of conservative treatment have occurred in children. Hence this treatment should be tried first, in such cases.

On the other hand, an operation is indicated if the patient is not responding to treatment, if the temperature remains raised and there is definite suppuration, and, particularly, if there has been a previous attack of sinusitis, or an acute exacerbation of a chronic sinusitis with severe pain. If the suppuration is confined to the nasal sinuses, an intranasal operation alone has been successful in spite of the oedema of the orbit. The difficulty is to be sure that there is no pus within the orbit, as a second operation to evacuate this abscess may be necessary.

Thirty-seven of the above-mentioned thirty-nine nasal sinus cases were operated on by the simple unheroic external operation, and adequate drainage was established into the nose. One slight case recovered without operation. Thirty-four of the operation cases made a rapid recovery and were highly satisfactory. One patient who had had a previous incision through the upper eyelid, already had meningitis when admitted, and died. A second patient died of superior longitudinal sinus thrombosis. A third, an emaciated and feeble elderly woman, died fifteen days after operation from almost a gangrene of the orbital contents.

The complications were few; in one severe case with a dilated pupil, the pupil subsequently developed optic atrophy and blindness in spite of a rapid recovery after his operation. It is interesting to note that in two cases of some duration optic atrophy developed. In one of the early cases the patient lost his eye owing to a corneal ulcer. In three of the cases there had been a simple incision before the operation described above was performed.

Summary.

About 72% of the cases of orbital cellulitis arose from nasal sinus suppuration. Orbital cellulitis and abscess is a dangerous condition, but there is a considerable variation of its severity.

The decision when to operate and whether an intranasal or external operation should be performed needs careful consideration.

When there is an orbital abscess the simple external operation should not be delayed.

The operation should be gently and carefully performed to establish drainage, with

counter-drainage into the nose. No radical operation, such as exenteration of the ethmoid, is necessary or advisable.

Thirty-four of the thirty-seven cases treated by the external operation made a rapid and satisfactory recovery. Two of the three fatal cases were doomed before the operation was performed. In the third fatal case, an intranasal operation was performed first and the external operation was too late.

BIBLIOGRAPHY

- BALLENGER, H. C. (1932), "Orbital Cellulitis and Abscess Secondary to Sinusitis", *Illinois M. J.*, **61**, 128.
 BABBITT, J. A. (1930), "The Diagnostic Problem in Orbital Cellulitis", *Tr. Am. Laryng., Rhin., and Otol. Soc.*, **36**, 225.
 GREENFIELD, S. D. (1934), "Acute Sinusitis in Children, associated with Orbital Complication. Conservative Treatment, Report of 10 Cases", *Laryngoscope*, **44**, 683.
 HITZ, J. B. (1933), "Management of Orbital Cellulitis Secondary to Sinus Infection", *Wisconsin M. J.*, **32**, 318.
 LAYTON, T. B. (1935), *Proc. Roy. Soc. Med.*, **28**, 1569 (Sect. Laryng., 49).
 LEWIN, J. (1930), *Brit. M. J.* (ii), 866.
 SCOTT BROWN, W. G. (1931), "Cavernous Sinus Thrombosis," *Lancet* (i), 960.
 SMITH, E. TEMPLE (1930), *Brit. M. J.* (ii), 14.
 WOLFF, E. (1929), "A Note on the Pathology of Orbital Hæmorrhage and Inflammation", *Tr. Ophth. Soc. U. Kingdom*, **49**, 195.

S. H. Mygind (Copenhagen): Acute cellulitis, or acute swelling of the orbit, has for many years been an object of special interest to me. In 1920 I published a paper, based on 35 cases, in the *Archiv. für Laryngologie*, **33**, 189; I have now also collected my cases for the last fourteen years. This period covers 86 cases of acute swelling of the orbit, which will be the basis of the following account.

EAR DEPARTMENT, COMMUNE HOSPITAL, COPENHAGEN

TABLE I.—121 CASES OF ACUTE SWELLING OF THE ORBIT.

1906-1920	35 cases (sinusitis 27, i.e. 77%)
1923-1937	86 cases (sinusitis 70, i.e. 81%)

TABLE II.—ACUTE SWELLING OF THE ORBIT.

1923-1937	86 cases
Morbidity somewhat higher than 1:100,000			
Mortality 16%			

Sinusitis 70 cases				Other origin, partly dubious, 16 cases			
Sex	40 ♂ - 30 ♀	Sex	4 ♂ - 12 ♀
Age	$\frac{1}{2}$ - 73, average 25 years	Age	$\frac{1}{2}$ - 65, average 23 years
Morbidity	circa 1:100,000				
Mortality	10%	Mortality	50%
(1906-1920)	26%)				

TABLE III.—SINUSITIS 70 CASES.

External operation	46 (7 dead)
Conservatively treated, or (in a few cases) endonasal operation	24 (0 dead)

TABLE IV.—46 CASES OF SINUSITIS VERIFIED BY OPERATION.

Ethmoid alone	13* cases,	1 dead
Front. sinus alone	5†	0
Max. sinus alone	1	1
Sphen. sinus alone	1	1
2 or more sinuses combined	26	4

* Osteoma of the ethmoid in one case.

† Osteoma of the frontal sinus in one case.

TABLE V.—26 CASES OF COMBINED SINUSITIS.

Ethm. + front.	16 cases
Ethm. > front.	...	9 1 dead	
Ethm. = front.	...	3 0 dead	
Ethm. < front.	...	4 0 dead	
Ethm. + max.	4 cases
Ethm. > max.	...	3 0 dead	
Ethm. < max.	...	1 dental (0 dead)	
Pansinusitis	6 cases
Perforat. from ethm.	...	5 3 dead	
Perforat. from max.	...	1 0 dead	

TABLE VI.—86 CASES OF ACUTE SWELLING OF THE ORBIT.

Sinusitis	Other origin	Total	Dead
Simple oedema			
Non-operated 24 }	6 1		0
Operated 11 }	3 1	44	2
Subperiorb. abscess	34	3	37
Phlegm. orbit. infl.	1	4	5
	70	16	86

TABLE VII.—COMPLICATIONS IN 63 CASES OF CURED SINUSITIS WITH ORBITAL SWELLING.

	Operated	Not operated
Post. ethm. cells, not opened at first operation	1	—
Osteoma	2	—
Tumour-like	2	—
Perf. in external corner of orbit	1	—
Slow pulse, slow cerebation	1	—
Trismus. Abscess in temporal region	1	—
Paresis sup. obl.	—	1
Meningismus + pleocytosis	—	1
Meningitis serosa. 23/3	1	—
No complication	52	—

TABLE VIII.—CAUSES OF DEATH IN 7 CASES OF SINUSITIS WITH ORBITAL COMPLICATIONS.

- 1 diabetes; erysipelas; sepsis.
- 1 thromb. sin. cavern., sin. sigm., vv. ophthalm. sepsis.*
- 1 perf. of cribrif. plate. Meningitis.
- 1 meningitis.
- 1 meningitis. Brain abscess. Aberrant ethm. cells with abnormal vascular pathways to the cranial cavity.
- 1 sepsis. *
- 1 meningitis. Brain abscess. No operation.*

4 meningitis. 3 sepsis.

* These three patients, admitted in a desperate condition, died within the first twenty-four hours.

TABLE IX.—16 CASES OF ACUTE SWELLING OF THE ORBIT, OF OTHER ORIGIN.

Cured (complication)	Dead (complication)
Traumatic	1 Brain abscess. Meningitis
Dental*	1 " " "
Osteomyelit.	2 (a) Epidural abscess "
(Frontal. zygom.)	(b) Thrbphlb. cavern. mening.
Facial	1 " " "
(Carbuncle)	
(Erysipelas)	
Tumour	
Dubious	3 (a) (b) Thrbphlb. cavern. mening. (c) sepsis.

* Besides 1 case of dental maxillary sinusitis.

An orbital cellulitis or orbital swelling is only present if there is an increase of the content of the orbit, causing a protrusion of the eyeball. In dubious cases the examiner should stand behind the bed-head of the patient, compare the position of both eyeballs from above, and determine, with one finger on each side, the exact relation to the supra-orbital margin.

It is often difficult—and sometimes even impossible—to decide whether a swelling of the orbit is caused by a sinusitis or not, even in fatal cases. A history of nasal discharge is often wanting. Often little or nothing abnormal is seen on rhinoscopy, and aspirating and syringing the nose—otherwise a valuable method—may reveal no pus. This may be owing to a closed empyema or to the causative sinusitis being slight. I have operated upon cases of subperiosteal abscess in which there was only a slight swelling of the mucous membrane, or pus only in a single small ethmoidal cell.

A skiagram is often difficult to procure, on account of the state of the patient and the want of time. Besides, the external swelling may disturb the result, and even a negative finding does not always exclude the presence of sinusitis.

When no sinusitis is found the cause is sometimes obscure. The origin may sometimes be a hidden nasal or sinus infection, especially in the ethmoid. In my former paper I have described some cases as probably due to a tenonitis. I have not seen such cases recently and now I should prefer simply to say that the orbit sometimes reacts in certain latent infections. In three or four cases there was a history of measles.

There is, further, no single sign which enables a distinction to be made between a simple collateral oedema and subperiosteal abscess. Abscess may occur at any age. It is not necessarily accompanied by fever, even in fatal cases. Localized tenderness of the orbital wall, tenderness of the eyeball itself, localized palpable infiltrations, pronounced chemosis, pronounced or localized fixation of the movements of the eye, displacement of the eyeball downwards or outwards, have all been regarded as signs of abscess in contradistinction to simple oedema. None of these symptoms singly is, however, decisive. That I have been able to be more conservative in the second than in the first period is only due to increased experience and better clinical judgment. One thing, however, I should like to point out, for which I am indebted to Professor Rønne, the ophthalmologist. In scarlet fever, in which orbital swelling of the most alarming proportions sometimes occurs, conservative treatment is nearly always successful. This recalls the spontaneous disappearance of the enormous glandular swellings of the neck after a scarlet-fever tonsillitis.

The presence of an oedema and not of an abscess does not always mean that operation is unnecessary. The sinusitis itself may indicate it, not to speak of later intracranial complications. Therefore, in the presence of alarming symptoms, rather operate once too often than wait too long.

Where the great danger lies is in the intracranial complications. These often evince no characteristic symptoms until too late. The frontal lobe of the brain is a dumb area and a meningitis only gives rigidity of the neck or Kernig's symptom, when it has reached the posterior fossa and so has become fatal. Therefore, on the slightest suspicion, especially on a sudden rise of temperature, a lumbar puncture should be performed immediately.

To the inexperienced operator I advise a wide incision of the orbit, permitting an extensive survey of its walls, to avoid the risk of missing an unusually situated perforation or aberrant ethmoid cells far back in the vault. In children under 5 years the frontal sinus is generally not yet developed, but otherwise I prefer to open not only the ethmoid, but also the frontal sinus systematically. We generally have to do with a combination of two or more sinuses.

The experienced operator, on the other hand, will often be able to get through with a small incision which will afterwards be hardly noticeable. It is surprising how good an exposure can be obtained by pushing the borders of such an incision in one or the other direction.

In osteomyelitis of the frontal bone, whether in connexion with a frontal sinusitis or not, the ordinary methods of operation do not allow a sufficient exposure to eliminate the whole affected area without leaving disfiguring scars and impairing

the action of the forehead. I have therefore made use of another method. A long incision is carried down to the bone, behind the borderline of the hair, from one ear to the other. The frontal part of the scalp is then turned downwards in one large flap, exposing the whole forehead. A few forceps are enough to arrest the bleeding. The diseased bone can be removed as radically as is necessary—forward as far as the orbital roof and the cribriform plate, and backwards as far as the sutura coronaria. It will often be necessary to remove the superciliary arch, and if so, the other side also has to be resected in order to obtain a satisfactory cosmetic result. The flap is put back in its original position, but only fixed very loosely by one or two stitches in the middle line. On both sides free drainage is established by gauze and india-rubber plates (made by splitting ordinary wide drainage tubes). After some days the incision in the aponeurosis may be further stitched by degrees. The final scar is concealed beneath the hair. The action of the frontalis muscle is preserved and the resected bone is reproduced. Only the profile is, in some cases, altered.

G. H. Howells: Orbital cellulitis may arise as an extension of an acute or chronic sinusitis. The commonest site of the primary infection is in the anterior ethmoid.

At first it is a pure cellulitis and is not localized by any well-marked line of resistance, except the periorbital which checks the spread of infection into the orbital fat. At this stage, therefore, it is unwise to embark on any drainage operation as by so doing one is running the risk of opening up fresh tissue planes which will become infected, with disastrous results.

One should, therefore, be as conservative as possible and endeavour to establish drainage of the sinuses by the natural route into the nose. The use of inhalations, sprays, &c., with puncture and lavage of the maxillary antrum, causes a reduction in the congestion and œdema of the mucosa of the mid-turbinate region and allows pus to escape. The antral puncture should be repeated daily and these measures will usually lead to a diminution of the orbital symptoms, the œdema and the displacement of the eye becoming less.

If suppuration ensues the abscess will be felt as a tense swelling at the inner angle of the orbit, behind and above the lacrimal sac. By this time localization of the infection will have taken place and one may safely drain the abscess through an incision around the inner angle of the orbit. The anterior ethmoidal cells are then opened into the orbit and the anterior one-third of the mid-turbinate is removed through the nose. This completes the first stage of the operative treatment in an acute case. In doing this one is only following the natural process of cure, as is seen in those cases in which the patient has allowed the abscess to burst externally, perhaps several times, before seeking advice.

The usual external ethmoidal or frontal sinus operation may be done two or three weeks later, when all dead bone must be carefully looked for and removed and all infected cells opened up.

When the condition arises as an extension of a chronic sinusitis the onset is usually less dramatic and suppuration occurs almost at once. The orbital swelling is therefore more localized and the general symptoms are less marked. Conservative measures are of no value in such cases and a radical exposure of the frontal sinus and ethmoidal cells must be carried out. The sphenoid should also be examined and, if infected, opened up and drained.

In young children suppuration rarely occurs if treatment is begun in an early stage. Resolution usually follows such treatment but a close watch must be kept for cerebral complications, as these may occur after the cellulitis has apparently subsided.

In cases secondary to osteomata of the frontal sinus or ethmoidal labyrinth, a

drainage operation should be performed and the tumour removed when the acute stage has subsided.

F. C. W. Capps: A patient cannot be considered to have orbital cellulitis unless proptosis is present, indicating an intra-orbital phlegmon or abscess. This will exclude numerous cases of œdema of the upper eyelid and supra-orbital region, associated with acute frontal sinusitis, in which there is no true involvement of the intra-orbital tissues. A large proportion of these cases clear up by the usual local and general measures or limited intranasal operations.

When, however, the globe of the eye is displaced, we are dealing with a spread of the infection beyond the bony confines of the original nasal disease. Test of displacement is described in Parson's "Diseases of the Eye" as follows:—

"The patient is seated, the surgeon standing behind him. The surgeon holds the patient's head in such a manner that he looks straight down the nose. He then rotates the head backwards until he can just see the apex of one cornea. If he can see more of the other cornea, that eye is relatively proptosed."

Suppuration is a definite indication for external operation, but it is often not easy to be sure that suppuration has occurred. When in doubt, I do not hesitate to incise the orbit, as there is no danger in so doing and with due precautions such incision leaves no disability after healing. In doubtful cases I prefer the approach favoured by ophthalmic surgeons in draining orbital cellulitis and leave the periosteum alone.

During the last two years I have been concerned in the treatment of seven cases of orbital cellulitis associated with nasal sinus disease. Of the seven cases in question, two were treated in the acute stage by orbital incision alone. Two others were treated by orbital incision and limited intranasal surgery but within a few days both had to have extensive surgical measures for osteomyelitis of the frontal bone and extra- and intradural abscess. The fifth case resembled the last two so closely in onset and appearance that I operated at once in a very radical manner.

The sixth and seventh cases were somewhat unusual, in that the orbital swelling and proptosis had appeared and disappeared before I was called in, although the condition of the patient in each case was becoming more grave. Owing to suspected intracranial complications, extensive surgery was carried out in these two cases.

(1) The first patient was a girl aged 21, with fourteen days' history of trouble around the left eye, attributed to such varying causes as a sty, a bee-sting, and sunburn. She was admitted under the ophthalmic surgeon, having a tender swelling of the whole orbital region and proptosis. There was no fluctuation. The left side of the nose was full of creamy pus and there was pus in the postnasal space. X-rays showed opaque left frontal sinus, ethmoids and antrum. W.B.C. 20,000. Culture gave a scanty growth of *Staphylococcus aureus*. I saw the patient the day after admission and advised orbital incision into the extraperiosteal tissues only. This was delayed for forty-eight hours and was then performed by Mr. Foster Moore and a glove drain was inserted. No pus was found. The next day the patient was very ill, vomited, and was incontinent of urine and faeces. On the fifth day she was delirious; on the sixth day she had two fits, with flexion of the left elbow, turning of the head, and conjugate deviation of eyes to the left. Dr. Chandler advised against lumbar puncture. On the seventh day she suddenly improved, became rational, and asked for food, and pus came from the wound. Recovery was uneventful. A fortnight later the left antrum was punctured and mucopus washed out. A fortnight after this it was again washed out and was clear and there was no sign of pus in the nose. She then attended hospital as an out-patient with the fistula sometimes closed and sometimes discharging. Four months later she was readmitted

and the left frontal sinus was cleared of granulations, débris and some small sequestra. The cavity was packed open with bipp; a fortnight afterwards it was clean, and the infundibulum was patent. Secondary suture. Two months later there was an abscess in the wound. X-rays showed for first time a sequestrum in the centre of the frontal region about half an inch above the highest level of the frontal sinuses. An incision was made over this area, the outer table of the skull was excised and part of the frontal crest which had sequestered was removed. The wound has remained soundly healed for over a year.

(2) In the second case, the patient, a woman aged 34, gave a history of chronic right-sided nasal trouble for over ten years, and of severe right hemicrania for several weeks. She was admitted to hospital, having pain and tenderness over the right antrum, right proptosis and oedema of both lids—greater of lower than of upper—papilloedema of both discs, and veins engorged on the right. X-ray examination revealed opacity of the right antrum and ethmoids and the lower part of the right frontal sinus. The proptosis increased and demanded an orbital incision and aspiration of the right antrum. Recovery was uninterrupted and a subsequent antrum lavage was clear. There has been no trouble of any sort for eighteen months.

(3) The third case was in a girl aged 20 who had toxic goitre and had had a partial thyroidectomy three months before. She walked up to hospital with acute right orbital cellulitis, after a history of one week's severe cold. At operation both frontal sinuses contained pus and on the left was a subperiosteal abscess spreading to the external angular process. Progress was complicated by thyrotoxicosis, and the patient seemed aphasic. Eight days later an extensive forehead flap was cut and osteomyelitic frontal bone was removed revealing extradural pus over the left frontal lobe. The patient died three days later. Post mortem, subdural collections of pus were found over the vertex, especially anteriorly and to the left and on the under surface of the frontal lobes, especially the left. Culture—haemolytic streptococci.

(4) The fourth case, in a girl aged 15, was rather similar. She had had influenza ten days before admission, and pain and swelling of the right eye for two days. The right frontal sinus was drained externally and the right antrum aspirated. Almost a week later a large flap and an extensive area of osteomyelitic frontal bone were removed. An extradural abscess and a leaking intradural abscess were found over the left frontal lobe. The rest of the history is mainly neurological and concerned with efforts to find intracranial pus, until the patient's death over two months later. She developed a large cerebral hernia on the left side, but for long periods was well and seemed to be recovering.

(5) The fifth case was sent up as one of renal oedema but the patient had a right orbital cellulitis and a temperature of 102° , after one week of aches and pains and no previous nasal trouble. She came within a week of the two previous cases and looked so like them that I at once turned the whole forehead back and removed the anterior walls of both frontal sinuses. There was pus under pressure in both of them but no evidence of spread to surrounding bone. Within a week all was clean and the infundibula were both patent.

(6) and (7) The sixth and seventh patients were children and both, when seen, had become very ill; one was comatose with neck rigidity, and cherry-coloured with septicæmia, and had a right hemiplegia, and the other was irritable and septicæmic and had a left hemiplegia and altered areas of sensation. They both had almost certainly a thrombosis of the superior sagittal sinus spreading to the cortex. In the girl, aged $6\frac{1}{2}$ years, I found a small deep frontal sinus full of pus on the side of the affected eye, and a bead of pus over the venous sinus, with some osteomyelitic bone. With open packing she made an amazing recovery and the wound fell in rapidly. When she was first seen there were 75 cells in a sterile cerebrospinal fluid.

The boy, aged 7, had a normal frontal sinus and no evidence of bone disease. Wide frontal decompression, however, improved his general condition greatly. Later

a puffy tumour developed over the vertex and when this was opened and diseased bone removed, a track of pus was found running deep down and to the right in the motor and sensory area. This patient is improving steadily.

E. Watson-Williams said he always maintained that there were two quite distinct states. In one there was infection—possibly actually an abscess—between the bony wall of the orbit and the periosteum, a peri-orbital abscess. There might be some palpebral oedema and chemosis, but the orbital tissues were not actually infected; in this condition the eye was of trivial importance, and the sinus disease and its possible complications dominated the situation.

It was far otherwise in the second class, in which actual infection of the orbital tissues led to cellulitis in the loose tissues and fat of the orbit, or to abscess formation therein. This was the true "orbital cellulitis"—a dangerous condition, not only because of the possibility of complications elsewhere, but also because of the threat of severe damage to the eye. Fortunately the second condition was much more rare than the first; he could recall dealing with only eight cases of it, and in two of these the sight of the eye had been lost before he saw the patient. In these cases early and active surgical intervention was essential.

The problem was, then, how to tell at the outset, when proptosis and palpebral oedema were present, which of these two very different conditions was responsible. His own teaching was that in peri-orbital infections, though the eye might be pushed forward, it was displaced also outward, or outward and downward; palpebral oedema was more in evidence than chemosis and there was, as a rule, only small interference with movements of the eyeball. On the other hand, when the orbital tissues themselves were the site of active infection, the eye was displaced mainly forward, chemosis was very conspicuous, and there was early great limitation of movement.

In such cases of true orbital cellulitis he had not had the opportunity of trying the effect of prontosil. His advice was to open the orbital tissues and, even if actual pus was not found, to insert a drain and then to employ heat, whether by kaolin poultice or the more fashionable ultra-short-wave treatment. Either helped to promote suppuration, which was what was needed. It might even be necessary to use more than one incision, to drain multiple abscesses.

W. Stewart said that he had been waiting to hear someone differentiate between the various organisms causing these affections of the orbit. It was necessary in a given case to decide whether a pus-forming organism or a streptococcus was present. If, with oedema of the orbit and a high temperature, a streptococcus was found, operation increased the danger. It became necessary to chase the organism throughout the head, with a strong chance that the patient would die. It seemed to him that streptococcal cases should not be operated upon and that they were suitable cases for the use of prontosil or serum.

W. S. Thacker Neville, referring to the recommendation to give prontosil, said it should be given in large enough doses; a person weighing 7 stones should be given 20 tablets of prontosil in twenty-four hours, or 100 c.c. of it in soluble form. The dose of the sulphonamide was calculated at the rate of 1 gm. for each 20 pounds weight, or 1 c.c. for each one pound up to 100 pounds, and 0.75 c.c. for each one pound up to 150 pounds in twenty-four hours. Two prontosil tablets three times a day was a quantity which he regarded as useless, as the dosages needed to be quite large. He considered that it was safe to give prontosil until the patient became blue, and this could be done in twenty-four hours.

He had in mind two cases of orbital cellulitis. One was in a girl who had double orbital cellulitis due to pansinusitis. She was in a toxic state and was very ill. It was

before the days of prontosil, and he had treated her with large doses of hæmolytic streptococcal serum—60 c.c. a day.

The other case was in a child aged 4 years, who had a cold in his nose on Sunday, and on Monday had proptosis of one eye and that eye was fixed. On Tuesday an eye specialist was called in and an incision was made in the orbit. On Wednesday the boy's father, who was a nose-and-throat specialist, had a skiagram taken and finding the sphenoid, antrum, and ethmoid opaque, proceeded to operate intranasally. The eye was blind and there were retinal hæmorrhages. After the intranasal procedure the proptosis did not subside, and, accordingly, after two days, an external operation was carried out: a perforation was found in the os planum, and a large abscess behind the eye. The patient was his (the speaker's) own son.

E. D. D. Davis (in reply) said that Dr. Mygind had spoken about the discrepancy in numbers between the ethmoid and the frontal sinus cases. If the abscess burst through the floor of the frontal sinus it was classified as a frontal sinus case, but probably the ethmoid was also involved. In children ethmoidal suppuration was more common than in adults. The antral suppuration was secondary to the ethmoidal disease.

S. H. Mygind (in reply) said there were three different stages of the condition: inflammation of the intra-orbital tissue proper, peri-orbital abscess, and simple swelling of the orbit. In the last there was not yet any infection of the orbit.

The condition which was most dangerous, as it was mostly fatal, was a real infection of the tissue of the orbit itself. In his series were four such cases, all of which were fatal.

He had operated on between 80 and 90 cases without having trouble from omitting to stitch the lids, and nearly all his cases were instances of infectious sinusitis. To omit opening thoroughly was dangerous. Experience showed that in some cases when there had been trouble afterwards, it was found that all the cells had not been opened.

The Relation of Upper Respiratory Tract Infection to Early Bronchiectasis in Children

By J. H. EBBS

RECENTLY I analysed a large number of post-mortem examinations in children, in order to determine the incidence of otitis media (1937). I was particularly impressed by the number of infants and young children who developed an upper respiratory tract infection followed by a more serious condition which usually resulted in the death of the child. One group which I found of particular interest included pneumonia and conditions related to it. These I have studied in some detail, following a similar plan to that of McNeil, Macgregor, and Alexander (1929), in their series of articles on "Studies of Pneumonia in Children".

The material for the observations which I wish to make in this paper has been gathered from 200 cases of pneumonia and related conditions, examined post mortem.

The result of examination of the sinuses and middle ears is shown in Table I.

TABLE I.—200 CHILDREN DYING WITH PNEUMONIA.

Sinuses infected	...	85	= 42.5%
Ears infected	...	133	= 66.5%
Sinuses and/or ears	...	160	= 80%

Of the cases 85 (42.5%) were found to have gross infection of one or more of the accessory nasal sinuses, while 133 (66.5%) showed evidence of purulent otitis media.

Of these 200 cases of pneumonia 160 (80%) had pus in the ears, or the sinuses, or both, at autopsy. Of the remaining 20%, five followed whooping-cough, one chicken-pox, one erysipelas, one laryngeal diphtheria, one tonsillitis and one retro-pharyngeal abscess.

This high incidence of upper respiratory infection found in children dying with pneumonia indicates that there must be some relation between the two conditions. Campbell (1934) studied one hundred and thirty patients with pneumonia, most of them young children, and he found that 100% had sinusitis, while 70% had an otitis media. Whether sinusitis and otitis media are significant factors in the aetiology of pneumonia or not, the high percentage of children who die with pneumonia, and have infection in the nasopharynx, is strong evidence in favour of a preceding, concurrent, or secondary upper respiratory infection.

Having found this high incidence of sinusitis and otitis media in this post-mortem series of pneumonia I decided to study them in relation to the end-result or actual pathology in the lungs and if possible to assess the importance of the infection in the nasopharynx. I was surprised to find a number of cases which showed more than ordinary pneumonia; in fact, chronic changes had taken place which allowed a pathological diagnosis of bronchiectasis to be made. The use of large paraffin sections—in some cases, of the whole lung—allows us to study the histology in all parts.

There are several types of bronchiectasis described, the classifications depending upon the aetiological factor, the type of dilatation or the extent of the disease. I do not propose to consider any but those which are the result of a respiratory infection which produces an ulcerative bronchitis. Severe or repeated attacks of bronchopneumonia account for the majority of cases in children. Boyd (1931) found that 30 of her 58 cases followed either bronchopneumonia or recurring or chronic bronchitis. Lemon (1926) reported 9 following bronchitis and frequent colds, 11 after pneumonia and 16 after disease of the nose, throat, or sinuses. He also found that 14 of 46 cases had a history of upper respiratory tract infection preceding the development of bronchiectasis, while 32 were found to have infection after the onset of bronchiectasis. Dennis (1924) found that of 60 patients examined with sinusitis, 24 had bronchiectasis and 28 were asthmatic. Whooping-cough and measles are the starting point of many cases in children.

The atelectatic type of bronchiectasis is usually difficult to trace to a definite onset in children. Sometimes it appears to result from an atelectasis which has been present since birth. It is also conceivable that in some cases it results from an atelectasis acquired during a mild attack of pneumonia or bronchitis. So-called bronchitis in infants often means that bronchopneumonia is associated with it, and complete occlusion of a bronchus by mucus could easily give rise to collapse of a small portion of a lower lobe, which eventually becomes bronchiectatic.

Age seems to play a large part in this disease. Boyd (1931) stated that most of her cases started before the age of two years. Moll (1932) found that 25% of his cases had their initial attack of pneumonia during the second year. Pneumonia is a frequent cause of death in children under 2 years of age and Table II shows that 85% were in this age-group, and 80% of them had an upper respiratory infection at autopsy. While all infants under 2 years of age do not die when they develop pneumonia, nevertheless the mortality is high. McNeil, Macgregor, and Alexander (1929) found this to be 44% in all cases of pneumonia in their study, who were under 2 years. Of those who survive, a large number must bear the scars of their lung disease. Jameson (1929) reviewed 58 children in London and Birmingham to determine the remote prognosis of pneumonia. These children had had the disease at some time in the preceding ten years and every attack had been of three weeks duration or longer. He found that only one-third were without symptoms, while one-third were suffering severe symptoms of pulmonary catarrh. He emphasized the danger of repeated attacks of pneumonia and periodic or persistent infections

from the upper respiratory tract, both of which could produce chronic pulmonary catarrh. Findlay and Graham (1931), discussing the prognosis of bronchiectasis, state that "recovery is more probable in the examples which develop during later childhood". This bears out the opinion that respiratory infections during infancy and early childhood are usually more severe, and produce more permanent damage. Examining a large number of sections in this series of cases of pneumonia, I found fifteen which showed dilatation of the bronchi and are examples of early bronchiectasis. Of these, ten—i.e. two-thirds—were from patients under two years of age.

The best study and summary of the pathology of bronchiectasis which I have encountered is the one by Erb (1933), who has shown all the changes which must

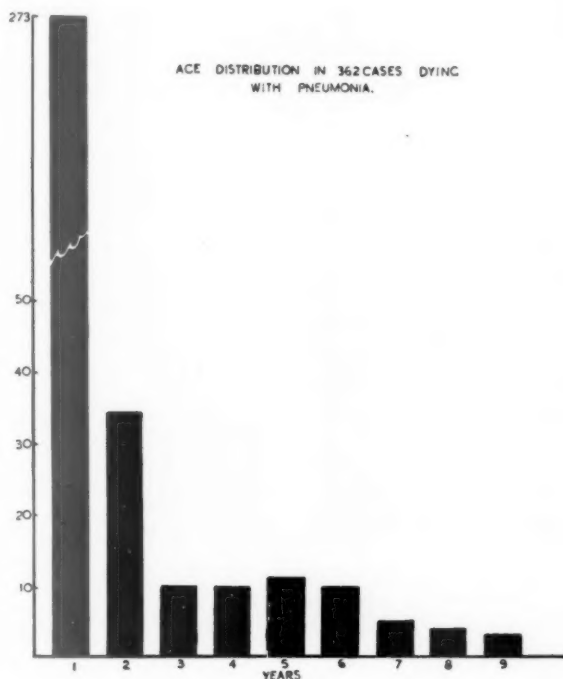


TABLE II.

occur in the lung, from the earliest inflammatory lesion in the bronchi until chronic bronchiectasis is well-established. He believes that the most important aetiological factor is infection of the bronchi and the presence of obstruction, which might be caused by thick exudate, swollen mucous membrane, or granulation tissue.

In the following illustrations of sections of lung from several of the cases which I have studied, there is a sequence of histological changes, varying in degree from acute bronchitis up to advanced bronchiectasis. Where chronic bronchitis in childhood ends and where bronchiectasis begins is impossible to say, since one gradually and insidiously merges into the other and throughout there is constant re-infection and advance of the process.

The section shown in fig. 1 was taken from a 20-months-old child, who had had pneumonia of two weeks duration. The illustration shows purulent secretion which is distending a bronchus; the mucosa is partially destroyed and the purulent exudate has broken through the wall and is involving the surrounding tissue. The muscle and elastic fibres are destroyed. This child had had several attacks of otitis media and bronchitis, the last attack resulting in pneumonia. Death was due to a purulent pericarditis.

In another child of the same age, with a history of a cough, otitis media, and cervical adenitis, for two months, the section showed a more advanced stage. Here the damage was more severe; the destructive process of the purulent infection was still going on, without any evidence of repair. The bronchi, in many places, were filled with purulent exudate which had ulcerated the epithelial lining and broken through the dilated bronchiole. The surrounding lung tissue was septic, collapsed and functionless.

In these two cases the process was that of a severe bronchopneumonia and ulcerative bronchitis. Naturally, all cases of bronchitis and pneumonia do not progress to bronchiectasis, but it is reasonable to expect residual damage if the child

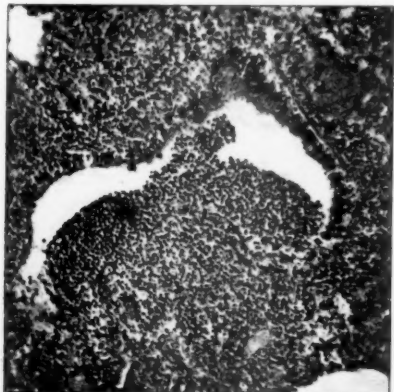


FIG. 1.

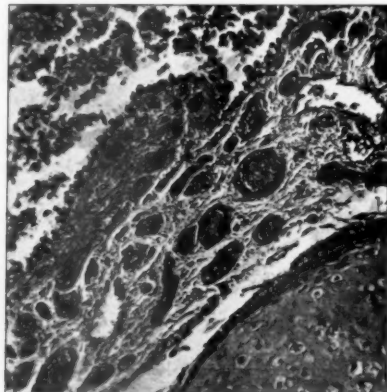


FIG. 2.

had survived. The severity of the bronchitis, the amount of obstruction or stagnation, the individual resistance, and the frequency of reinfection of the diseased areas, seem to be the factors which determine the ultimate pathology.

In the section shown in fig. 2 there is evidence of a new, flatter type of mucous membrane laid down on organized granulation tissue. The cartilage plate in this section is the only element of the bronchial wall which has not been involved. Fig. 3 from the same case shows how the muscle fibres have been destroyed in one area and new granulation tissue is forming a ridge or protrusion into the lumen. These ridges of granulation tissue, which are devoid of normal ciliated epithelium, are a cause of obstruction. This child developed otitis media at the age of 6 months, followed by bronchitis, which recurred about every three weeks. She was admitted to the hospital as a possible asthmatic, with wheezy breathing. She died soon after admission in an asphyxial attack, and at post-mortem we found saccular dilatations of both lungs, some fibrosis, enlarged tracheo-bronchial glands, and purulent exudate in the bronchioles. There was a chronic otitis media and purulent infection of the maxillary antra.

Fig. 4 shows a somewhat similar condition, although the chronic changes were not so marked. A 5-year-old girl swallowed lye in infancy, was treated for oesophageal stricture, and later developed a chronic bronchitis. A fatal acute laryngitis developed about three years after the onset of the bronchitis. The bronchi here showed various degrees of dilatation and there was fibrosis. In this section a bronchiole has had its lining epithelium ulcerated away, it has been acutely dilated and now the exudate is becoming organized. This is the only case which did not show gross evidence of infection of the middle ears or sinuses. The oesophageal stricture and chronic bronchitis are the only antecedent factors found.

Fig. 5 (p. 66) is a low-power photograph of a section of the lung of an infant who had a chronic cough for nine months, after otitis media which developed during convalescence from a successful operation for pyloric stenosis when three weeks old. The dilatation of the bronchioles is extreme in the left lower lobes, and inflammatory changes were still going on in the bronchial walls. Here again otitis media and sinusitis were found post mortem.

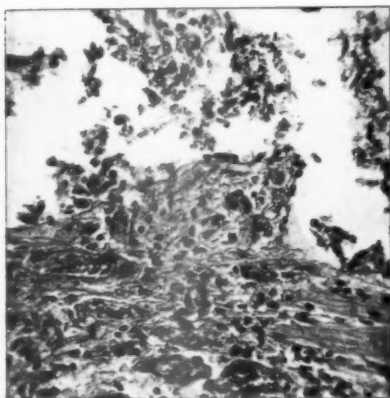


FIG. 3.

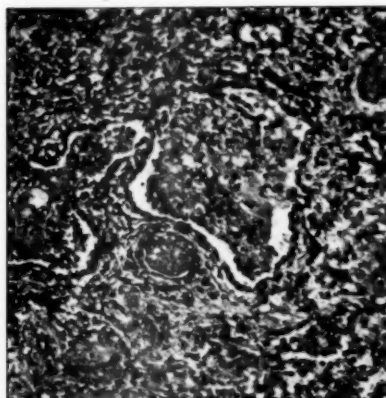


FIG. 4.

A 14-months-old infant developed bronchitis and otitis media at the age of 3 months and was left with a cough which continued until death occurred, rather suddenly, from a brain tumour. There was not time for terminal pneumonia to develop and therefore the condition in the lungs was interesting. There was evidence of an early bronchiectasis, and of a purulent infection of both middle ears, the maxillary antra and the ethmoid cells. Cultures from these revealed haemolytic streptococcus and *B. influenzae*. There was organized granulation tissue present in the maxillary antra and sections of the mucous membrane showed a chronic infection. In the section (fig. 6) dense infiltration with polymorphonuclears and ulceration of the epithelium lining the antrum can be seen. A section taken from the lung showed dilated bronchi with evidences of fibrosis surrounding them. It is reasonable to suppose that the sequence of events in this lung has been an early bronchitis or possibly pneumonia, which has never completely resolved and has been constantly stirred up by fresh infections from the upper respiratory tract. Probably the first dilatation was a functional one which has become permanent by the action of toxins and the stagnation of purulent secretions, which have destroyed the normal function of the bronchial wall and allowed fibrosis to fix the bronchi in a permanently dilated

condition. Moll (1932) says that in the early stages of bronchiectasis the condition may be simply a loss of tone of the bronchial wall, leading to temporary dilatation.

The next few illustrations demonstrate Nature's poor attempt at repair and show the varied pathological picture in more advanced bronchiectasis. The first is taken from a marked case of bronchiectasis, with clubbing of the fingers, in a child aged $11\frac{1}{2}$ years. The sections are taken from the left lower lobe which was removed suc-

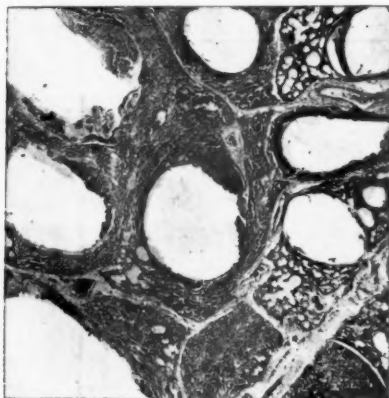


FIG. 5.

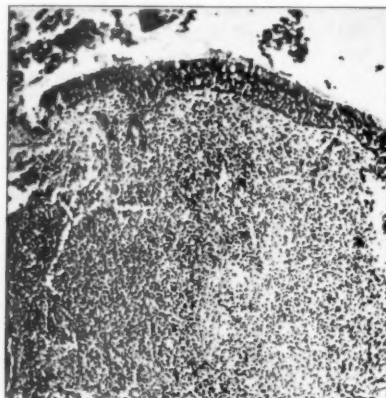


FIG. 6.

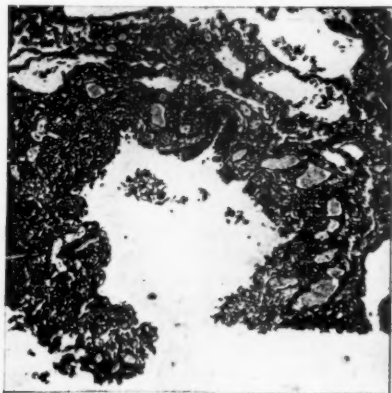


FIG. 7.

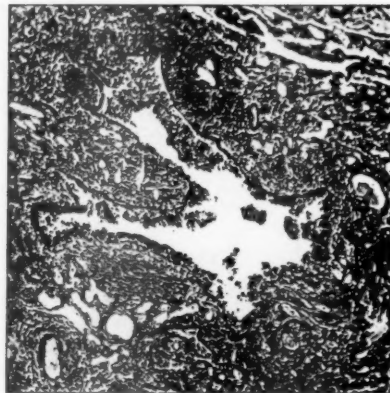


FIG. 8.

cessfully, with an apparent cure. The first (fig. 7) demonstrates the extensive damage which is going on in a more recently involved bronchus. The mucous membrane is almost completely ulcerated away, numerous dilated capillaries surround it and there is evidence of a chronic purulent infection destroying the elements of the bronchial wall. This also demonstrates that the condition is a progressive one and that different parts of the bronchial tree may be involved successively.

Fig. 8, taken from the same case, shows a large tongue of new granulation tissue projecting into the lumen of a dilated bronchus, which has retained or regenerated normal columns of epithelial cells showing a few cilia. The epithelium covering the granulation tissue is squamous and is composed of a single layer only. The next section (fig. 9) is of a large dilated cavity surrounded by fibrosis, with loss of muscle and elastic fibres. On one side there is hypertrophied epithelium in folds, and on the other there is a flatter type of epithelium, with evidence of ulceration. Areas of granulation tissue such as this and the tongue in fig. 7 are probably the source of frequent hæmoptysis.

Fig. 10 shows the lung of a 7-year-old girl who developed a bad cold, which persisted, with an ever-increasing cough, until she died of pneumonia one year after developing the upper respiratory infection, showing how rapid the progress of the disease can be.

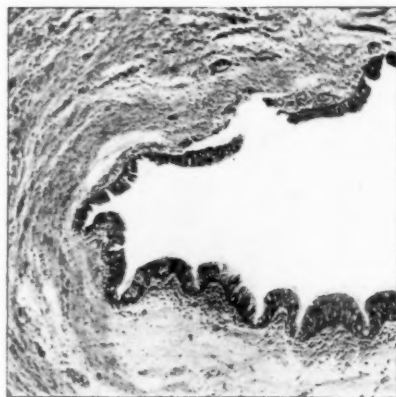


FIG. 9.

In all of the fifteen cases of early or chronic bronchiectasis which I have found in this series—except the one with œsophageal stricture—there was purulent infection of the sinuses or middle ears. That this infection might have been secondary to the bronchiectasis I cannot deny. The history of onset with upper respiratory tract infection is significant, however. The part which sinusitis plays in the progress and chronicity of bronchiectasis can best be described as a vicious circle. This whole point is well summed up by Lemon (1926)—

"From a study of the relationship of disease of the accessory sinuses, evidence has been produced showing that such disease may be the van or rear attack, the cause or result of bronchiectasis."

In conclusion I wish to make two general statements about treatment. It seems evident from my study of these cases that the pathology of bronchiectasis points to the hope of relief of symptoms, and possibly, of cure, if treatment is instituted at an early stage. When the chronic stage of this disease is reached, the only hope of complete recovery is the removal or destruction of the diseased area. My other point is with regard to climate. The vast majority of cases occur in the poorer classes. We need a great many more convalescent homes and hospitals in the country or at the sea, to which city children suffering from chronic bronchitis, or

convalescent from pneumonia, can go. Our recent experience of having a convalescent branch in Switzerland has proved that it is in the above group that the results have been far beyond expectation. Many of them have shown a continuation of their restored health for a period of two or more years.

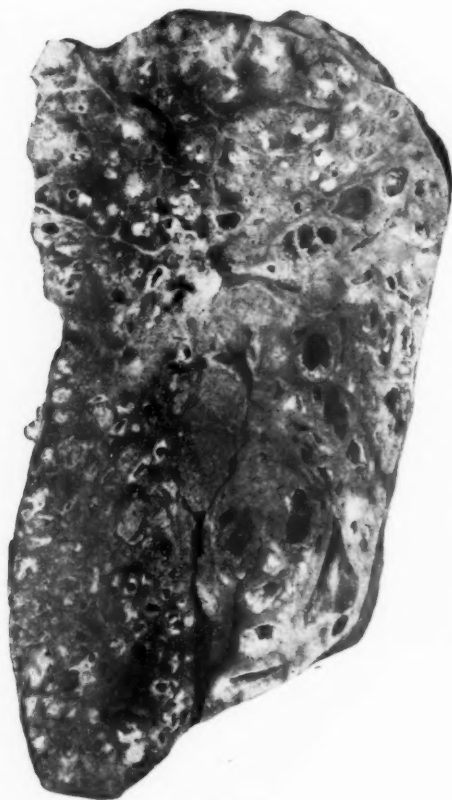


FIG. 10.

A greater appreciation of the incidence of sinusitis and otitis media in infancy, and the possibility of chronic lung changes which might result from bronchitis and pneumonia, together with the hope that earlier treatment and better convalescence will reduce this disease, are the points which I have gathered from this study.

REFERENCES

- BOYD, G. (1931), *Canad. M. A. J.*, **25**, 174.
CAMPBELL, E. H. (1934), *Arch. Otolaryng.*, **20**, 698.
DENNIS, F. L. (1924), *Ann. Otol., Rhin. and Laryng.*, **33**, 451.
EBBS, J. H. (1937), *Proc. Roy. Soc. Med.*, **30**, 1297. (Sect. Otol., 53).
ERR, I. H. (1933), *Arch. Path.*, **15**, 357.
FINDLAY, L. and GRAHAM, S. (1931), *Arch. Dis. Childhood*, **6**, 1.
JAMESON, H. P. (1929), *Arch. Dis. Childhood*, **4**, 365.
LEMON, W. S. (1926), *M. Clin. North America*, **10**, 531.
MCNEIL, C., MACGREGOR, A. R., and ALEXANDER, W. A. (1929), *Arch. Dis. Childhood*, **4**, 12.
MOLL, H. H. (1932), *Quart. J. Med.*, N.S., **1**, 457.

The Relation of the Ear, Nose, and Throat to the Diseases of Children

By BRANFORD MORGAN

As in infants the most important factor in life is nutritional, so by a nutritional disturbance do they react to any derangement of health. When an infant who is obtaining sustenance of sufficient caloric value, with the correct proportions of essential and accessory food factors, fails to thrive, or develops some gastro-intestinal disorder, an infection must be sought. It is within recent years only that the importance of infection outside the gastro-intestinal tract has been realized. Apart from syphilis and tuberculosis, the common infections arise from the upper respiratory and urinary tracts and from the skin; of these, infections of the upper respiratory tract vastly preponderate.

A simple rhino-pharyngitis in itself may suffice to cause refusal of feeds and vomiting-and-diarrhoea in a healthy infant, and its effect will be much more serious on a child admitted to hospital for an already established disorder. That this problem of upper respiratory infection in infants is urgent, had already impressed me, but during this recent winter it has done so more than ever. Not only have we lost cases admitted for apparently simple feeding difficulties, but in several cases of congenital pyloric stenosis the patients have fallen victims in the post-operative period. That our experience is not local is shown by the title of a recent leader in the *Lancet* (1937 (i), 39) entitled—"The Danger of being admitted to a Children's Ward". Continental and American authorities have insisted upon the almost constant infection of the ears resulting from a nasopharyngitis in the infant, and debate has been devoted to the relationship between otitic infection and gastro-enteritis.

It is realized that the silent otitis media is not specific to cases of gastro-enteritis; we find it during the course of many of the acute infections, such as pneumonia and pyæmia, and in chronic diseases, such as scurvy and syphilis, whilst post-mortem examination shows that in a large proportion of infants who have died from various causes, infection exists in the mastoid.

It is, however, the relationship between gastro-enteritis and ear infections that I wish to hear discussed. Is the ear infection—so frequently the sole post-mortem finding in a marasmic child—simply a terminal event, part of a terminal septicæmia which may occur in any disease? is it a secondary effect caused by vomitus spreading up to the Eustachian tube? or may it be the primary cause of the disease or a complicating factor which maintains and exacerbates the nutritional disorder? In the papers and discussions which have appeared recently on this subject I have failed to find any help in diagnosing mastoid disease in these small infants. The value of radiography is emphasized by some writers, but there is no general agreement on this point. However rapidly and expertly the operation may be performed, such interference may well weigh the scales against the precarious existence of these infants.

I have heard that in some clinics a rapid exposure of the mastoid is performed in practically all cases of marasmic and enteric disorder which fail to respond to myringotomy, but although I am ready to admit that I have had successes myself in such cases, I have never felt satisfied that such wholesale operation is justifiable until we have more evidence than we now possess of a specific and primary relationship between otitis and nutritional disorder, and more knowledge of when the mastoid is infected.

We may here consider nasal sinus disease—another frequent complication of upper respiratory infection, and here again it is doubtful whether this condition in children has received the attention it merits. We meet with nasal sinusitis as a cause of

continued pyrexia, the recurrent head cold and the chronic cough, and in diseases of the lower respiratory tract such as asthma and bronchiectasis.

During every influenza epidemic cases are seen of children who, having shared in the family epidemic, fail to regain a normal temperature. This continued pyrexia often leads to parental anxiety that the patient is tuberculous. The pyrexia is usually irregular, the child remarkably well, with a "stuffy" nose and perhaps some mucopus coming down from behind the soft palate, a loose cough, usually worse at night. Such cases generally clear up with a menthol inhalation, a nasal spray, and a visit to the sea, but sometimes the course of the illness is more stormy, being complicated by tonsillitis and otitis, giving support to the statement that tonsillitis is often the result of a sinus infection.

Then there are the children brought to us because they are constantly catching cold; a certain number of them have allergic rhinitis, but many have latent infection in the sinuses, in which with each reinfection, the ostia become congested and drainage is obstructed; there is a rise of temperature, with, perhaps, headache and stuffiness which abate on relief of the congestion and institution of free drainage.

To state that chronic sinus disease is a cause of general debility is, I think, putting the cart before the horse, I prefer to look upon the child debilitated by illness, by undernutrition, by faulty environment, as lacking in resistance to upper respiratory infection. As a result of the inflammation and irritation of the pharynx from the post-nasal discharge, a chronic cough may result. When the discharge is free the cough is loose, but when the discharge has ceased and only the pharyngeal irritation remains, the cough is dry and frequently associated with croup, which is difficult to distinguish from a diphtheritic laryngitis. Too little attention has been paid to non-diphtheritic types of laryngitis in young children, in whom severe and even fatal dyspnoea and cyanosis may result from an upper respiratory infection usually of streptococcal nature.

As an outpatient physician I diligently sought for and enthusiastically advised operation upon infected nasal sinuses in asthmatic and bronchiectatic patients, but although a temporary improvement might occur afterwards, the ultimate results were disappointing. In asthma the sinus infection is doubtless due to the turgescence of the mucous membrane, resulting in blocking of the ostia and prevention of satisfactory drainage. Although operation is disappointing I feel that it should still be advised to ensure efficient drainage of the sinus.

In bronchiectasis there may be more hope of obtaining results by treatment of the sinus infection, as it is a reasonable hypothesis that infection of the upper respiratory tract may result from disease of the lower.

The majority view, however, is that the whole respiratory tract is simultaneously infected, and the condition is suggestively styled by Wasson "broncho-sinusitis". Bronchiectasis has well been described as a disease of childhood and certainly a large number of adult sufferers date their symptoms from childhood. The importance of pulmonary atelectasis, as a precursor of bronchiectasis, has been emphasized by many writers.

In whooping-cough, tracheo-bronchitis, and bronchopneumonia in young children, atelectasis is a constant feature, and it is well recognized that bronchiectasis in adults frequently dates back to such respiratory disease.

The relationship between tonsillitis and the triad of arthritis, chorea, and carditis which constitute the rheumatic infection, has long been recognized, and the frequency with which its manifestations are preceded by a tonsillitis can leave no reasonable doubt of a connexion between them. Vast amounts of work and argument have centred around the identity of the organism responsible, and the consensus of opinion is that rheumatic infection is due to a hæmolytic streptococcus of no specific strain; it has been shown that the serum of children suffering from acute rheumatism contains a higher titre of anti-hæmolysin capable of neutralizing the hæmolytic

toxin of streptococci than does the serum of normal persons—indicating that rheumatic subjects have been previously infected with these organisms. Another important fact is that sore throat preceding rheumatism is liable to occur in epidemics, and that a latent period of 10-21 days occurs between the attack of tonsillitis and the rheumatic manifestations, during which period the child is apparently well. This evidence is sufficient to concede a relationship between throat infections and the rheumatism of childhood.

It would be excusable to expect that children whose tonsils have been removed would be less liable to rheumatism, but this beneficial result is doubtful. In the investigation of a large series of cases the conclusion was reached that tonsillectomy may possibly render an individual less liable to rheumatic arthritis, and therefore possibly, to carditis, but certainly not to chorea. Disappointing as the results of tonsillectomy are in offering any control of the rheumatic state, the fact is quite intelligible, because tonsillitis is simply part of an infection of the whole throat and post-nasal space, and removal of tonsils does not reduce the liability to such infection. This conclusion is borne out from another angle, it having been shown that the incidence of droplet infection was no less in children whose tonsils and adenoids had been treated surgically. Similarly nephritis, which is often a sequel of a sore throat, is not affected in its progress by removal of tonsils.

Discussion.—S. H. MYGIND said that in some cases the changes in the drum membrane were only slight in children. In his younger days he had seen children who had a rise of temperature which could not be explained, and when he was consulted he had said there was nothing wrong in the ear; yet on the day after the child was examined a discharge from the ear had begun. An important question was how the inflammations and infections found in the lower air tract, stomach, and intestines were related to the ear condition and to each other. Was it likely that the inflammation found in the sinuses, the ears, the pharynx, and the tonsils, caused the trouble in the intestinal tract? It might be so, but more often the processes in the different parts arose at the same time from the same general cause.

It was often difficult, in dealing with children, to know whether a high temperature was due to the ear condition, or to the pulmonary or bronchial condition, or to glands in the neck. With the passing of the years he had become more conservative in his attitude. He seldom performed tonsillectomy in children, because the young child needed a certain amount of lymphatic tissue. When the patient was seen years after tonsillectomy he certainly had not the tonsillar complaints that he had had previously, but he was sometimes troubled by a dry throat and cough, with, perhaps, a trickling of mucus. At this later date the granules on the posterior wall were red, and in some a new tonsil had developed, even in cases in which the operator was sure he had removed the lower part of the tonsil. Those facts argued in favour of the view that in the growing organism the lymphatic tissue should be conserved in the throat as much as possible.

In children, whether they had diseases in the nose, the throat, or the ears, the principal thing was not the surgery, nor the specialist treatment, but the general treatment, including nutrition, fresh air, skin, bathing, and light baths.

F. C. ORMEROD said he was interested in the relation of bronchiectasis to sinus disease in children. He dealt with bronchiectasis in children who had survived the acute stage, passed into the chronic stage, and come up for lobectomy. It was his function to ascertain whether they had an upper respiratory infection which kept up the chest condition. There was no preponderance of sinusitis in these cases, and otitis was comparatively rare. In most of the cases of which Dr. Ebbs had spoken the patients had died, but the original cause was probably an acute rhinopharyngitis, causing pneumonia and spreading in the other direction to the sinuses and ears—the conditions being coincident rather than causative.

He only occasionally saw a discharging ear in connexion with bronchiectasis, and though the tonsils were often enlarged, sinusitis was not common, nor was nasal or oral suppuration leading to bronchiectasis.

In adults, a very large proportion of lung abscesses seen by him and his colleagues at

Brompton Hospital followed an operation on the mouth or nose, or some disease in those regions which had been treated surgically.

In these cases of acute inflammation of the respiratory tract in children, he advised that great care should be taken in operating on the upper parts of the tract, or chest complications might be precipitated rather than avoided.

DOUGLAS GUTHRIE said that Dr. Ebbs had pointed out how sinusitis and otitis could play a part in the aetiology of bronchiectasis. Did he not regard sinusitis and otitis as themselves secondary phenomena? Was not the true primary infection adenoiditis or tonsillitis? It had been said that after removal of tonsils and adenoids there was more liability to lung infection.

Both papers had laid stress on general treatment—climatic, nutritional, hygienic. Those connected with convalescent hospitals or children's hospitals must have noticed how well the infections of the upper respiratory tract cleared up when the child was placed under better conditions.

The common cold, which might be annoying and disabling in the adult, was really dangerous in the infant, as it was invariably accompanied by bronchitis and bronchopneumonia.

Dr. Morgan had mentioned the absence of otoscopic evidence of otitis in infants. There was often an absence of redness and bulging of the membrane, but there was always an absence of the light reflex, though the membrane might otherwise look normal.

The general view of otologists in this country was that it was useless to open the mastoid process in cases of gastro-enteritis in infants.

N. W. MACEKITH said that in the Southampton Children's Hospital there had been an outbreak of diarrhoea in children in one ward, and inquiry revealed that it had often begun in children who had no nasopharyngeal infection.

Although many cases were encountered in which both the ear and the alimentary canal were infected, giving rise to otitis media and gastro-enteritis, he regarded these as concurrent manifestations of the same general infection; it was a mistake to infer that the otitis media was the cause of the gastro-enteritis.

T. RITCHIE RODGER said that in an investigation by Mr. R. R. Simpson, in the Children's Hospital at Hull, in sixty cases a bronchoscopic examination was made at the request of Dr. Morton Stewart, the physician, who said that chronic coughs had practically been eliminated from his clinic. Perhaps physicians elsewhere would give the laryngologist the chance to prove the value of bronchoscopic treatment in cases of bronchiectasis. The treatment consisted of aspiration, and, in most of the cases, the insertion of gomenol through the bronchoscope. About 15 per cent. of the cases were said to be associated with active sinus disease. It seemed reasonable that if an early bronchiectasis was present, aspiration once a week should cure many cases before they arrived at a higher degree of dilatation.

J. H. EBBS (in reply) said that Mr. Ormerod and he were not on the same track. He agreed that otitis media and bronchiectasis were not frequently associated. The point that he emphasized was the high incidence of otitis media and sinusitis in pneumonia and early bronchiectasis in young children. In fully developed bronchiectasis, infection was invariably found in the sinuses. Whether the infection was the primary cause or was coincidental infection, he did not know, and it was impossible to say. In the 15 cases of early bronchiectasis which he had studied, there was, with one exception, a history of upper respiratory infection at an early period.

It had been his impression, from a pathological study of these cases, that aspiration with the bronchoscope offered as much hope as anything else.

B. MORGAN (in reply) said he agreed that the association of sinus disease and bronchiectasis was frequently found in children. In adults, too, in a large proportion of cases of bronchiectasis there was also sinus disease.

The result of sending patients so affected to Switzerland was very striking; their sputum cleared up in a remarkable manner, but when they came back to this country the symptoms often returned.

As good results were obtained by postural drainage as by aspiration, to remove bronchiectatic material, especially if the Nelson bed was used, and patients could be got to sleep with the head inverted. Bronchoscopy must be distressing to the young child, and he presumed it was carried out without an anæsthetic.

JOINT DISCUSSION No. 5

Section of Physical Medicine with Section of Obstetrics
and Gynaecology

Chairman—GEOFFREY HOLMES, M.B. (President of the Section of Physical
Medicine).

[March 19, 1937]

DISCUSSION ON THE SPA TREATMENT OF
PELVIC DISORDERS

Dr. Muriel Keyes: The modern observation [1] of the increased hormone contents in the blood-serum and urine of women after mineral-moor baths suggests that endocrine stimulation—rather than (as hitherto thought) solely thermal causes—may be the underlying reason for ancient belief in these mineral-moor baths. And as a vegetable hormone folliculin-like substance is present in mineral moors, so perhaps these may yet be found in solution in some mineral waters?

Modern spa therapy means the varied use of “fresh natural waters” and muds “at or near their source”, an individually adjusted régime of diet, exercise, and rest, with the psychologic aid of change of air and scene, and respite from household or business stress.

British gynaecologic spa therapy, as compared with that on the Continent, suffered a partial eclipse by the rise of surgery.

Our amenities were rarely mentioned, even in our own medical journals, while many continental spas constantly and clamorously reiterated their peculiar special virtues; only Woodhall Spa advertised internationally its ability to treat the diseases of women [2], yet we were not shy to stress our claims to treat delinquencies on the part of the liver, kidneys, intestines, or circulation. One wonders if our omissions arose merely from national modesty as to our clinical capabilities, for Bath, recently shedding some of its reticence, yet cloaked a gynaecologic advertisement in French! [2]. British spas can treat British women as well as any continental spa, but unless we tell our own patients so in plain English then they will continue to “go abroad where they specialize in this”. My function now is to show the general application of natural, spa, hydro- or physio-therapy in gynaecology and the value of British hydrological methods, not to discuss either the well-known merits of physiotherapy (electricity, &c.), or even the link between adolescent virginal leucorrhœa and chronic, or recent, pelvic sepsis in nulliparous or parous rheumatics, though the interest of such observation is never-ending.

Close co-operation is essential between the patient's doctor and the spa physician. Patients should either (a) come with their case diagnosed and completely investigated bringing clinical history, pathologic reports, and indication as to the type of help sought from spa treatment, whether before operation, instead of it, in attempt to avoid it, or after; or (b) be “sent” for treatment and investigation, or warned that investigation at the spa may be considered helpful or even necessary.

A year never passes at a spa but one or two patients coming for relief of pain are found, on investigation, to be suffering from unsuspected malignant disease, and have to return as unsuitable—which is unfortunate.

Unless needful investigation is made either at home or on arrival, spa-treatment savours of quackery and mere "peddling" of baths and waters.

As in other spa therapy, gynaecologic treatment is both general and local; general treatment (through metabolism) aims at putting the whole patient in the fittest state possible; local treatment is directed to the disease manifestation—(local exudates and thickenings—uterine engorgement or flabbiness, pudendal skin conditions, &c.).

While hæmorrhage-debilitated or recent convalescents require treatment to help anabolism, the under-exercised obese, the inert chronic toxæmic, the menopausal myalgic need catabolic speeding-up to aid elimination (their reno-cardio-vascular condition being duly assessed); the intermediate types require corresponding treatment, and any type may need local treatment to the pelvic organs also.

General treatment.—(1) The drinking of fresh natural mineral waters at or near their source.

(2) Application of waters at varying heats and force: (i) Externally as baths, sprays, jets, and water packs. (ii) Internally as douches, to bowel and vagina.

(3) Application (at varying heat and thickness) of baths and packs of mud, peat or fango, the diluent being either mineral or tap water.

Local treatment.—(1) External: Application of waters at varying degrees of heat and force by jets, sprays, douches, or partial baths (i.e. half-sitz), and of mud, peat, or fango packs, poultices, or partial baths.

(2) Internal: Lavage to bowel, and vagina (here of varying heat and duration) of mineral waters, or, if only the effect of simple heat or mechanical action be desired, tap-water may be used.

Bowel lavage, as well as water drinking, is essential in chronic pelvic sepsis or pelvic congestion, to speed elimination of general toxæmia, &c.

(3) Combined external and internal: As prolonged hot vaginal douche *during* external application of pelvic pack (mud, peat, &c.), wet compress or half bath; or an undercurrent douche at one temperature played on abdomen or pelvis during total immersion in a bath at another temperature (immediately following internal lavage (bowel or vaginal), given *before* the bath).

To avoid the giving of vaginal douches in communal bath-tubs I prescribe douches to precede the medical baths (from both the æsthetic and the hygienic standpoint). Every women's bathing-treatment centre should have simple douching-tables or spray-bidets, adjacent to the bath-cabinets, for use as a matter of course in cases with vaginal discharge, just as preliminary foot-washing is enforced before entering swimming baths. Intestinal lavage, an essential part of spa gynaecological treatment, should be easily accessible.

Vaginal douches are a valuable means of applying prolonged internal heat in acute adnexitis, chronic pelvic infection, or trauma left by the latter, and can be a practical proposition in an out-patient department, as shown by Professor Statham in Bristol. But douches should only be given as a definite course of treatment properly prescribed, and not haphazard, for years, at the patient's whim.

General treatment acting through the skin upon the central nervous system and the general circulation can, according to the temperature, force, and duration, stimulate blood- and lymph-flow and general metabolism, diluting toxins and speeding elimination by skin, lungs, kidneys, and bowel, or have the soothing, relaxing effect needed in cardio-vascular or mental disease.

Local treatments; "packs", hot or cold, affect local circulation, whereas *water treatments* can combine the heat-massage-effect of jets, sprays, and continuous douches with the simpler cleansing action of removing waste (vaginal and bowel lavage); or the sedative effect of a soothing "undercurrent douche" (a jet of water played *gently* on a part already immersed in water) can be employed.

Drinking waters.—My experience is limited to the sulphur and iron waters of Harrogate.

The sulphur waters are usually divided into three classes, (1) strong saline, (2) mild saline, and (3) alkaline sulphurs; the irons (chalybeate waters), into saline chalybeates, and pure chalybeates.

Sulphur waters are both aperient and intestinal antiseptics, having definite action upon liver and gall-bladder, can be taken over a long period without depressant effect, probably because of the presence of barium.

The iron (in ferrous form) of chalybeate waters (which also contain manganese) is often tolerated where oral medicinal iron is not.

Types of cases responding to spa treatment :—

(1) The flabby, pale girl with irregular, scanty, or painful menstruation, often constipated and toxæmic, and possibly under-developed or overgrown, with poor stance and atrocious posture.

(2) Young mothers exhausted by hæmorrhage, hard labour, or sepsis (frank or occult); the older chronic endometritic with excessive menstrual loss, and xanthorrhœa, perhaps with joint or muscle rheumatism commencing; other cases showing pelvic scarring, prolapse, or chronic pelvic sepsis with discharge.

(3) The climacteric with general vasomotor or mental distress.

(4) The unhappy victims of pudendal pruritus (menopausal, senile, or caused by discharge) with or without local furunculosis, dermatitis, leucoderma, or other local changes.

(5) Vaginitis due to the *Trichomona vaginalis* appears to respond to "strong sulphur water" douching, but experience is yet limited.

Any one of these classes may approach the borderline mentally, particularly the pruritic, and while in the so-called "neurotic constant backache woman" the factors of dyspareunia, coitus interruptus, lack of synchronism, &c., must receive psychologic help, yet a physical lesion must also be sought. If these patients are examined, how frequently are found a cervicitis, gaping or torn cervix, uterine ligaments slack or fibrosed, with sunken vaginal roof; bad posture following pregnancy (lordosis or poor general tone), fibrositis as marked in the pelvic lining as in muscles outside, while skenitis and chronic urethritis explain dysuria, frequency, and poor urethral control.

The surgical gynaecologist, feeling surgery not justifiable in these cases, often dismisses them as neurotic or says there is "nothing wrong"; the patients, harbouring a real sense of grievance, wander into the hands of quacks—yet many would respond to suitable spa treatment.

In spa gynaecology a wide (general) women's experience kept continually alive by (special women's) hospital experience, together with an honest mind, and meticulous care in both examining and history-taking, is absolutely necessary. Better to refer many cases back for independent examination, or refuse them spa treatment outright, than that one case of doubtful malignancy should suffer delay in suitable treatment; also "the evil that we (spas) do lives after us—the good oft interred with our bones".

A woman is what she is by the sum total of her internal secretions; so a woman with uterine sepsis is a septic woman and not only the womb but the whole woman needs to be treated, and both conservative and surgical gynaecologists would find that a preliminary spa course of baths and waters would put their patients in a better local and general state for further treatment or operation, and that their surgical cases would normalize more quickly after a post-convalescent course.

References.—1 VOGT, "Hormones in Moor Baths", *Arch. M. Hyg.*, October 1934, 12, 291. 2 *Arch. M. Hyg.*

Dr. Leonard Boys: Patients with certain gynaecological diseases have been treated at Woodhall Spa for well over fifty years with results which have found favour with many of the leading gynaecologists of the time. Successful surgical treatment

has reduced the number of cases so treated, but there must still be a large number of cases of chronic inflammation of the pelvic organs, and borderland surgical cases, in which spa treatment should be of great value.

The treatment at Woodhall consists of baths and vaginal douches of the bromo-iodine waters or mud packs to the pelvis and vaginal douches.

Cases of peri- and para-metritis, sterility from congestion of uterus or ovary, sub-involution, and certain cases of fibroids have been successfully treated.

Such cases are often associated with colonic stasis and the patient's general health as well as the local conditions are often favourably influenced by colonic irrigations.

There is also a type of case in which, so far as can be determined, there is only disturbed function (possibly, as Dr. Theobald suggests, there may be a menstruation centre in the brain which in such cases fails to control harmoniously the hormones of the ovaries and anterior pituitary). It is generally believed that such cases are best treated by hygienic and dietetic methods to which might well be added spa treatment in general without particular application to the pelvic organs.

Professor Daniel Dougal: The persuasive eloquence of the two previous speakers has not convinced me that it is either necessary or desirable to extend the scope of physical methods of treatment in the way they suggest.

Physical treatment is probably the oldest form of therapy and was extensively employed in gynaecology, as in other branches of medicine, right up to the beginning of the modern surgical era. Since that time its popularity has declined, but this is not owing to any surgical bias on the part of those who practise gynaecology but to its failure to produce results in any way comparable with those which we are able to obtain by surgical methods. That being so, it would obviously be a retrograde step, and contrary to the best interests of our patients, to recommend physical treatment for conditions which we know can be better and more quickly dealt with by means of a surgical operation.

There are, however, a number of pelvic disorders for which surgical treatment is either unsuitable or insufficient, and in many of these physical methods are of great value and should be employed whenever possible. To obtain the best results the treatment should be carried out by a physiotherapist, but he should realize that his position is ancillary and that he should only treat patients who have been referred to him by a gynaecologist. I would apply the same rule both to the physiotherapist who specializes in gynaecology and to the gynaecologist who specializes in physiotherapy, because neither of them can have sufficient experience of diagnosis or of alternative and possibly better methods of treatment.

Physical treatment may operate in two ways, either by improving metabolism—and through that, the different functions of the body—or by acting directly on certain diseased structures. In obstetrics and gynaecology the first method is undoubtedly valuable, but the second has a more limited application and is much less satisfactory.

I must now refer to some of the pelvic disorders for which physical treatment has been suggested or recommended, and it will be convenient if I divide them into functional disturbances and organic lesions, although I realize that this classification is by no means watertight.

Functional disturbances.—In every case of disturbed function the general health should receive first consideration and all possible measures be taken to restore it to normal. The fact that the reproductive function is controlled by anterior pituitary and ovarian hormones, and that it is now possible to employ these therapeutically, detracts in no way from the truth of this statement, because all such treatment is substitution-therapy and cannot permanently restore the endocrine balance.

A modern and well-equipped spa has all the necessary facilities for the purpose and is eminently suitable for patients who can afford it, but the cases should be

carefully selected and the treatment carried out on general lines and not specifically aimed at the pelvis.

Patients with secondary amenorrhœa, or menorrhagia, associated with a gouty or rheumatic tendency, will probably benefit from this treatment, but dysmenorrhœa and disturbances of the menopause may be made definitely worse. Dysmenorrhœa is often cured or relieved by correcting the patient's mental outlook and teaching her to regard menstruation as a natural function and not as a disease and therefore, unless there is associated anæmia and debility, it is quite wrong to send her to a spa, where the whole atmosphere may tend to confirm her belief that she is really ill.

The same objection applies in the case of patients suffering from menopausal disturbances. These women should be treated with some preparation of œstrin and encouraged to lead a normal life; otherwise they may become confirmed invalids and a nuisance both to themselves and to their families.

In dysfunctional hemorrhage or metropathia the disturbed menstrual cycle may possibly be corrected by a combination of spa treatment and hormone therapy, but exploratory curetting is necessary to determine the type of metropathia and also to exclude the possibility of organic disease.

Mechanical lesions.—The stretched and weakened abdominal walls resulting from pregnancy can be largely restored by a course of massage, and this should be carried out as a routine during the puerperium. Similarly, gymnastic exercises which strengthen the pelvic-floor muscles are a useful prophylactic measure in reducing the incidence of genital prolapse. This displacement is extremely common and is responsible for a great deal of invalidism, but it can be readily cured by means of a vaginal plastic operation.

Uncomplicated backward displacements of the uterus rarely produce symptoms, but when they do are best treated surgically.

Infections.—Physical methods of treatment have achieved considerable success in the cure or amelioration of infections of the female genital organs, and it is in this field that they can be most usefully employed.

Acute and subacute infections of the lower genital tract should be treated expectantly, the parts being kept at rest and free drainage promoted; meddling treatment at this stage will almost certainly drive the infection into the higher regions of the pelvis.

On the other hand, chronic infections require more active treatment, but unless there is a grossly diseased cervix which can be amputated or cauterized it is extremely difficult to effect a permanent cure. I am convinced that the vagina, not the cervix, is the source of the discharge in many of these cases, and that frequent irrigation with bland fluids and the efficient application of heat are more rational methods of treatment than the use of antiseptics, which still further damage the vaginal walls.

Acute salpingitis is now treated expectantly, as active surgical treatment results in a much higher mortality and also interferes with the complete recovery of the diseased structures which occurs in a considerable percentage of cases. Subsidence of the acute attack may be followed by disappearance of all symptoms and even by complete restoration of function, but in less favourable cases the disease may remain persistently subacute, there may be recurring acute attacks, or the patient may complain of symptoms of a chronic character, due to the residues of infection.

In the subacute type, usually associated with pelvic exudates, heating-up of the pelvis is of great benefit in aiding absorption and restoring mobility to the diseased organs, and this should be carried out in consultation with the physiotherapist.

Recurring acute attacks are usually the result of reinfection either from the lower genital tract or from an infected partner and may be prevented or minimized by improving the patient's resistance and instructing her to avoid violent or prolonged exercise or excessive or unprotected intercourse.

Patients who complain of chronic pelvic pain, dysmenorrhœa, dyspareunia, menorrhagia, or persistent vaginal discharge, may also be kept in a reasonable state of health by enforcing similar restrictions, but whether this is practicable or desirable in either case will depend very much on the patient's social position and mental outlook. If she is a working-class woman with a husband and family to look after she will probably prefer the short cut to complete recovery offered by a surgical operation, but if she is in a better social position and not greatly concerned about her domestic responsibilities I can well imagine that the atmosphere of a pleasantly situated spa will prove so agreeable that she may decide to remain there indefinitely. My own practice is to advise surgical treatment when there are gross lesions in the pelvis and the patient is in danger of becoming a chronic invalid.

So far I have been speaking of severe pelvic infections, but minor degrees are often met with and may or may not be responsible for the symptoms complained of.

First of all there is the patient with developing rheumatoid arthritis in whom it is important to find the septic focus responsible. Not infrequently there is some evidence of uterine infection and then it is quite justifiable to treat the local condition when the patient is receiving spa treatment. Many of these cases are improved by amputation of the cervix and this is the method which I prefer.

Then there is the multiparous woman who is always tired and who also complains of backache, menorrhagia, and vaginal discharge. She has a damaged infected cervix, but there is also a considerable degree of genital prolapse. No doubt such patients would be benefited by so-called detoxication of their pelvis, but the only way to cure them permanently is to amputate the cervix and perform a double colporrhaphy. Amputation is superior to other methods of treating the cervix in these cases as it prevents the subsequent development of cervical carcinoma.

New growths.—Physical methods have no value as a curative measure in the treatment of uterine fibroids and may be actually harmful if they delay necessary surgical treatment.

The surgical treatment of these tumours is so successful that it would be foolish to depart from our present practice and adopt methods which at their best are only palliative.

Physical treatment before and after operation.—I am quite sure that many of our patients would become better surgical risks if they received a course of spa treatment before operation, but it is doubtful if the slight improvement in our results would compensate for the delay and expense involved. The badly exsanguinated patient who requires an operation can be treated just as efficiently with hæmatinics, or better still, by blood transfusion.

The average patient who has undergone a major operation returns home at the end of three weeks and is then placed under the care of her family doctor and instructed to take things easily for another month or so. An intermediate period at a spa hospital would certainly be beneficial, if the treatment were so planned that it hastened the patient's convalescence and did not actually prolong it.

My views on the subject of physical treatment may appear somewhat pessimistic, but they are coloured by what I have seen of spa gynaecology as practised in foreign clinics. I am convinced that if the method became popular in this country many serious pelvic lesions would be overlooked and a great number of minor ailments treated with more respect than they deserve.

Mr. J. D. Barris: We advise many patients suffering from minor pelvic disorders or debility to take a course of treatment at a spa, preferably British. But, while this is true, we must make it quite clear that our object in sending them has been for the beneficial effects upon their general health rather than for the specific effect on their local condition.

Moreover, we regard close co-operation between the physiotherapist and the gynaecologist as essential. All patients should first be seen by a gynaecologist in order to establish their diagnosis, to make sure that no serious pelvic lesion has been overlooked, that necessary surgical treatment should not be delayed, and to determine the type of case suitable for spa treatment.

To consider now some of the conditions which the physiotherapist has advanced claims to benefit. For example :—

Dysmenorrhœa.—We regard the functional type of dysmenorrhœa as quite unsuitable for spa treatment. The patient is usually a young woman and is perfectly well between her periods. It is essential to her recovery that she should be encouraged to lead a normal healthy life, that her mind should be taken away from her pelvis, and that she should not regard herself as an invalid, as local methods of treatment and the atmosphere of a spa might tend to suggest.

All dysmenorrhœa is not functional. It may be due to endometriosis of the ovary or tumours of the uterus, for which surgery or radiological treatment give the best results.

The menopause.—We also regard patients undergoing the menopause as quite unsuitable for spa treatment. They can be best helped by encouraging them to lead a normal life, and by the administration of œstrin. Such patients are often depressed, and self-centred. It is essential that they should be taken out of themselves and not be allowed to concentrate upon their own symptoms, otherwise there is a real risk that they may sink into real invalidism and their life become a misery.

Irregular bleeding.—Here spa treatment may do good by improving the general condition, but it should not be directed to the local condition, for this may be due to so many other factors—such as endocrine dysfunction, metropathia hæmorrhagica, or fibroids—which are best treated surgically.

In cases of irregular bleeding curetting may also be necessary to establish the diagnosis and exclude malignancy.

Vaginal discharge.—Erosions and cervicitis may be helped by douches or sprays, but these local measures are only useful in washing away the accumulated discharge. They fail to cure the condition, for the infection is too deep seated. Treatment by diathermy or, if the cervix is also damaged, by amputation, will give better results.

Pelvic inflammation.—Local heat undoubtedly does good in such cases, but surgery is needed in all cases of an acute nature, or where pus is present.

Pelvic pain without physical signs.—In these cases the patients certainly benefit by local heat measures, but the type of patient must be chosen carefully. It is difficult to assess the pain in many instances. Many patients of this type seem to have bad health and always have a pain somewhere. Such patients again are quite unsuitable for spa treatment, for they are often fleeing from the realities of their lives, and their pain is only a psychological barrier raised against their duties, which are unpleasant to them. To send such patients to a spa does not really help them, and may even do them harm.

But when all is said it is only right to add that there remain certain cases of a gynaecological nature which may derive benefit from treatment at a spa. Our only quarrel with our friends who carry out this treatment is that they are extending their methods too widely. Professor Dougal's remarks seem to me to represent quite fairly the views held by gynaecologists at the present time.

Mr. Clifford White said he thought that treatment at some spas produced a beneficial alteration in the menstrual rhythm in certain patients, but he could not agree that local treatment to the pelvis was desirable in many of the conditions mentioned by the opening speakers. As an example, loss of control of urine ("stress incontinence") was associated with a definite anatomical lesion, and the only logical

treatment was to restore the original condition of the urethra by a plastic operation. Another disease mentioned as suitable for spa treatment was senile vaginitis; this was now successfully treated by giving oestrin. With regard to the anæmic, constipated, flabby girl with dysmenorrhœa, it was certainly desirable that the anæmia and constipation should be treated at a spa or elsewhere, but it was undesirable to lay stress on a girl's pelvic organs by any local treatment that had to be repeated on numerous occasions.

Dr. A. Mougeot (Royat): The spa treatment of gynaecological disorders has been given in France for over twenty centuries. In that country there are about 250 well-equipped spas, a few of which are specially devoted to gynaecological cases. The names of some of these are literal translations of Latin names—a fact proving the antiquity of hydrological practice (*Chaudes Aigues* = *Caldas Aquas*; *Aix-les-Thermes* = *Aguas Thermas*).

Four kinds of water are used, each related to a special type of disorder. Hyper-thermal radio-active hypotonic waters are best for those cases in which there is severe pain but slight—if any—organic lesion. Saline and cold water, containing up to 25% of chlorides, are most efficacious in the treatment of fibroids, often eliminating the necessity for castration. When a young patient is under our care, it is of great importance to give medical treatment, because though the immediate result of castration is eminently satisfactory, the patient presently becomes a chronic invalid owing to the endocrine imbalance caused by the loss of the ovarian hormones.

Hot sulphur waters are specially indicated for septic oophoritis, which often yields to the treatment so successfully that after a short course a patient may become pregnant—the patency of the Fallopian tubes having been completely restored.

The fourth type of spa is that in which the waters are warm and contain a great deal of carbonic acid; such waters are not found except in volcanic soils. This is the only type of spa of which I have personal experience. The waters are specially suitable in cases of uterine atony with poor circulation and vascular stasis and also in cases of fibrositis of endocrine type.

A previous speaker has expressed the fear that spa treatment at the time of the menopause may induce a feeling of chronic invalidism. There is no doubt some ground for this fear, but on the other hand, when a high blood-pressure consequent on the cessation of the periodic discharge is threatening cerebral hæmorrhage and heart failure, it is essential to take the greatest possible care of the patient, and spa treatment should certainly not be neglected. Again, in cases of serious cardiovascular disorders associated with the menopause, treatment at a spa should be advised.

The fact that certain of our spas in France, though devoted entirely to the treatment of gynaecological disorders, are in a flourishing condition, proves that in the considered judgment of gynaecologists this treatment is remarkably efficient.

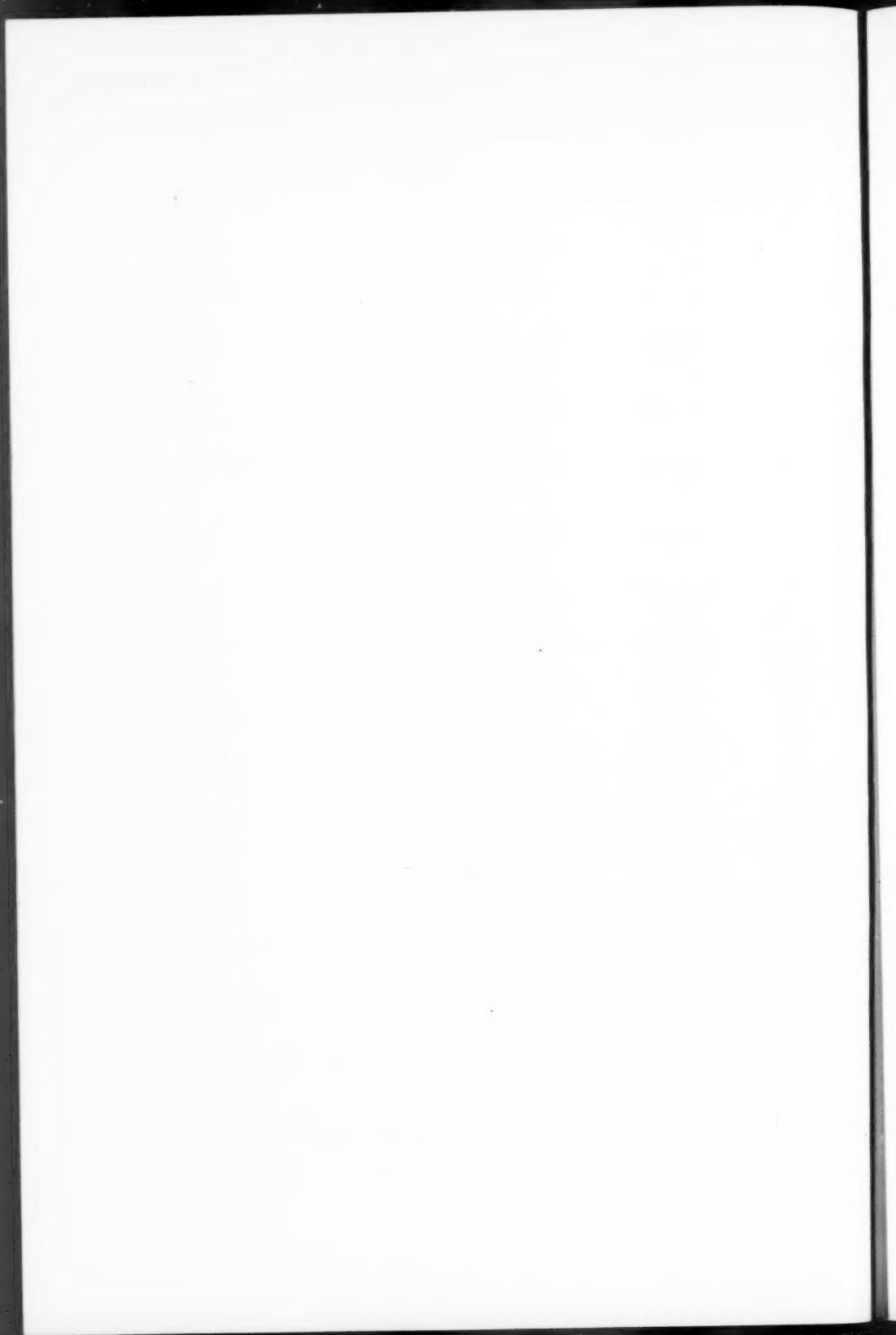
Recently spa-therapy in France has been improved with regard to thermal treatment in two ways: (1) Subcutaneous injection of sulphurous mineral water (an improvement which leads one to think that the efficiency of the water consists in strengthening the defensive powers of the whole organism rather than in a local microbicidal action). (2) Dry baths of spontaneous gases emerging from the springs, the patient being put into a gas-tight sack. This practice began in my own spa and has been very successful. I was led to its introduction by the conviction that the value of the water is largely due to the spontaneous absorption of thermal gases through the skin during a bath.

Dr. Geoffrey Holmes (Chairman) said that he could confirm the statement made by Dr. Muriel Keyes, that no spa practitioner of repute would attempt to treat by physical methods cases unlikely to be benefited by such treatment. It not

infrequently happened that growths and other serious pelvic disorders were first discovered during the routine general examination which the patients received at a spa, and that whenever necessary the spa practitioner saw to it that the advice of a gynaecologist was obtained.

With reference to Dr. Mougeot's account of the widespread use of the French spas in the treatment of pelvic disorders, he would point out that French doctors, and indeed medical men in practically all continental countries, were taught the principles of spa treatment and were expected to know which spas were indicated for various ailments. The absence of such teaching in many medical schools at home was detrimental to patients and doctors alike, but the fact needed stressing that there were spa waters in this country, and facilities for their application, which made it quite unnecessary for patients to be sent abroad to obtain spa treatment for pelvic disorders.

The fear had been expressed that a visit to a spa was likely to encourage the development or continuation of chronic invalidism. This fear was not justified by practical experience. One of the main objects of spa treatment was the creation of an environment in which the patient could be restored as rapidly as possible to mental as well as physical health and well-being.



Section of Urology

President—BERNARD WARD, F.R.C.S.

[May 27, 1937]

Observations on Genito-urinary Tuberculosis

By JAMES CARVER, F.R.C.S.

ABSTRACT.—Early and reliable diagnosis is obtained by cultural methods.

Pyelographic evidence of renal destruction is necessary as a rule to supplement the positive laboratory findings before resorting to nephrectomy.

Bilateral renal tuberculosis should not be diagnosed on the findings of cystoscopy alone.

Nephro-ureterectomy is the ideal operation. It prevents the prolongation of the bladder symptoms and the breaking-down of the operation wound and the risk of another operation for the removal of the ureter, not forgetting the danger of infection of the other kidney.

Bad results are probably due, in the case of poor patients, to economic and sociological factors which interfere with restoration to health after operation.

Genito-urinary tuberculosis is to be regarded not as a localized disorder but as a manifestation of a generalized disease, a fact which necessitates a guarded prognosis and prolonged after-treatment.

RÉSUMÉ.—Les méthodes culturelles rendent possible un diagnostic précoce et certain.

Avant d'entreprendre une néphrectomie il est généralement nécessaire de faire un examen pyélographique pour compléter les signes positifs de destruction du rein obtenus par les méthodes de laboratoire.

Le diagnostic de tuberculose rénale bilatérale ne doit pas être fondé sur une simple cystoscopie.

L'opération idéale est la néphro-urétérectomie. Celle-ci empêche la prolongation des symptômes partant de la vessie et la rupture de la blessure opératoire, et, par conséquent, évite le risque d'une nouvelle opération pour l'excision de l'uretère, sans oublier le danger d'une infection de l'autre rein.

Chez les malades pauvres les mauvais résultats sont probablement dus à des facteurs sociaux ou économiques qui nuisent au rétablissement après l'opération.

La tuberculose génito-urinaire ne doit pas être considérée comme maladie locale, mais comme l'expression d'une maladie généralisée, ce qui nécessite un pronostic réservé et un traitement post-opératoire prolongé.

ZUSAMMENFASSUNG.—Frühzeitige und zuverlässige Diagnosen lassen sich durch bakteriologische Methoden erzielen.

Bevor man sich zur Nephrektomie entschliesst ist in der Regel der pyelographische Nachweis der Nierenzerstörung zur Ergänzung positiver Laboratoriumsbefunde notwendig.

Die Diagnose doppelseitige Nierentuberkulose sollte nicht allein auf Grund des Cystoskopiefundes gestellt werden.

Die ideale Operation ist die Nephro-ureterektomie. Durch sie lässt sich eine Fortsetzung der Blasenbeschwerden sowie das Wiederaufgehen der Operationswunde und auf diese Weise das Risiko einer weiteren Operation vermeiden; nicht zu vergessen ist dabei auch die Gefahr einer Infektion der anderen Niere.

Schlechte Resultate, wie man sie im Falle armer Patienten sieht, sind wahrscheinlich auf ökonomische und soziologische Faktoren zurückzuführen, die die postoperative Wiederherstellung der Gesundheit gefährden.

Tuberkulose der Harn- und Geschlechtsorgane sollte nicht als eine lokale Störung, sondern als Ausdruck einer Allgemeinerkrankung aufgefasst werden; dies bedingt eine vorsichtige Prognose und lange Nachbehandlung.

THESE observations are founded on 46 cases which have been under my care during the last four years. No attempt will be made to discuss all the aspects of genito-urinary tuberculosis, but I will confine my remarks to the problems that these cases presented and their interpretation in the light of current urological teaching. Nearly all the cases were sent from sanatoria where they were undergoing treatment either for tuberculosis of the urinary tract or tuberculosis of the lungs and joints. There were 28 cases of renal tuberculosis, 10 of genital tuberculosis, and 8 with tuberculous bacilluria.

Table I bears out the well-known fact that renal tuberculosis is most common during the second, third, and fourth decades. In a recent series of 1,571 cases collected by Ekehorn there were 1,225 between the ages of 21 and 50.

Table II shows the incidence of tuberculosis in other parts of the body and illustrates the generalized nature of the tuberculous infection.

Table III gives the classification of patients with renal tuberculosis. In six cases, one of which was my own, in which nephrectomy alone was performed, the resulting condition was not satisfactory. In three empyema of the ureteric stump, and in two empyema of the stump and tuberculosis of the opposite kidney, developed, and in the sixth case there was a complete breakdown of the operation scar. In the last but one in the series nephro-ureterectomy had been performed and the patient was left with a persistent tuberculous cystitis.

Table IV is of the patients who suffered from genital tuberculosis. The occurrence of the disease during the period of most active sexual activity is seen and also the widespread nature of the tuberculous trouble. You will notice that in Cases 4, 6, and 9 tubercle bacilli were found in the urine, but no renal lesion was detected on cystoscopy and pyelography.

TABLE I.—CASES OF RENAL TUBERCULOSIS.

Age					Sex
0—10	No cases
11—20	2 males, 3 females
21—30	6 " 5 "
31—40	7 " 3 "
41—50	1 male
51—60	1 "

TABLE II.—RENAL TUBERCULOSIS—TWENTY-EIGHT CASES.

Presence of Extra-renal Tuberculosis.

	Active 9	X-ray evidence 7	Total 16
Lungs	" 1	Old Pott's disease 1	" 2
Pott's disease	1
Lungs and spine	1
Lungs and glands	2
Lungs and joints	6
No evidence found	

TABLE III.—CLASSIFICATION OF CASES OF RENAL TUBERCULOSIS.

Tuberculosis of the kidney	16
Bilateral renal tuberculosis	3
Empyema of ureteric stump following nephrectomy	3
Empyema of ureteric stump with tuberculosis of the opposite kidney	2
Tuberculosis of the kidney with hydronephrosis of the opposite side	2
Persistent tuberculous cystitis following nephrectomy	1
Breakdown of kidney wound after nephrectomy	1

TABLE IV.—GENITAL TUBERCULOSIS—TEN CASES.

No.	Age	Condition of renal tract	Other tuberculous lesions
1	35	No tubercle in urine	No evidence
2	24	Tuberculosis of kidney	Tuberculosis of lungs and knee
3	29	Bilateral renal infection	Spine, cervical glands
4	27	Tubercle in urine. No renal lesion	Lungs
5	39	Tuberculosis of kidney	"
6	31	Tubercle in urine. No lesion detected	"
7	23	Kidney	Hip
8	48	Nil	Lungs
9	21	Tubercle in urine. No lesion found	Ankle and spine
10	24	Right kidney	Hip and lungs

TABLE V.—GENITAL TUBERCULOSIS.

No.	Site	Rectal examination under spinal anæsthetic	Treatment and observations
1	Left castration 1925. Tuberculous right epididymis, 1926	Nil	Operation refused—general health very good. Sanatorium treatment
2	Bilateral epididymitis within six months of nephrectomy for tuberculous kidney	Nil	Admitted with broken down renal wound. Sanatorium treatment
3	Left epididymis	Prostate and vesicles involved	Died. Generalized tuberculosis
4	1934—Epididymitis with sinuses which healed. 1935—Left epididymitis with discharging sinuses	Nil	Left epididymectomy—right side not touched. Sanatorium
5	Tuberculosis of right epididymis and testis	Nil	Castration. Sanatorium
6	1933—Right castration. 1936—Left vas deferens ligatured elsewhere	Nil	Sanatorium. Very good health
7	Tuberculous epididymis and testicle	Nil	Castration
8	Tuberculous epididymis and testicle	Nil	Castration
9	Castration, right—1934. Castration, left—1935	Nil	Sanatorium
10	Left epididymis 1936. Right epididymis 1936	Nil	Sanatorium

Table V shows the distribution of the infection in the seminal tract. It will be observed that half of the cases had bilateral epididymitis, the second epididymis becoming involved within a year of the first. In three the testis was so diseased that castration was necessary, and in one bilateral castration had to be performed. Thomson-Walker stated that the second epididymis was invariably involved within a year, but in a recent series of cases reported by Barney, only 10.6% had infection of the opposite side after epididymectomy.

All these cases were examined rectally under a spinal anæsthetic. In only one was there evidence of prostatic and vesicular disease; on urethroscopy this patient was seen to have prostatic abscesses opening into the urethra. The male patients in the renal series were also examined rectally and no evidence of tuberculosis of the prostate or vesicles found. The primary site in the seminal tract is one that has been contested for years. Young supports the theory of Guyon that the first lesion is in the vesicle, and he reports 50 cases of genital tuberculosis in which the prostate and vesicles were involved in all, the epididymis on one side in 14 and on both sides in 31. Simmons, as quoted by Barney, states that in 200 autopsies the primary focus was

in the prostate in 50%, and in 25% of the cases, in the vesicles and epididymis. Kraemer criticizes Simmons' findings and points out that as all these patients were submitted to autopsy they were all of necessity advanced cases, and that the multiple foci in the genital tract might as well have been produced by the original lesion as by the genital lesion.

Out of 57 children suffering from tuberculous epididymitis Kantorowicz reports only two in which the prostate was involved, and Barney reports six cases of tuberculous epididymitis in infants, in five of which he could find no discernible lesion of the prostate or vesicles. Cunningham makes a most important contribution to the subject: In a series of 4,250 necropsies at the Boston City Hospital there were 35 cases of tuberculous epididymitis, and a careful examination of the prostate and vesicles was made in all these cases; in 25 the prostate, vesicles and epididymis were involved, but in 10 the epididymis alone was affected. In 1930 Lowsley and Duff could only collect from the literature one case in which the prostate alone in the seminal tract was the seat of the tuberculous lesion. The exposed position of the epididymis would make it more liable to injury than either the prostate or vesicle, and the connexion between injury and tubercle is well known. Another point one might advance in favour of the epididymis containing the initial lesion is the anatomical similarity between the seminal and the urinary tracts. The epididymis and the kidney discharge their secretions into a receptacle through a duct and in both ducts the middle portion suffers least or not at all, and removal of the kidney and epididymis has a beneficial effect on the bladder and vesicle. The results of epididymectomy on the prostate and vesicles do not bear out the theory that the primary lesion is other than in the epididymis. For instance, in 69 cases out of 113 which Barney followed up and in which the prostates were nodular and tender before epididymectomy, rectal examination showed that the vesicular and prostatic condition had either disappeared or considerably improved. Primary tuberculosis of the prostate and vesicles is almost unknown post mortem, and Bothe states that there is only one specimen of a primary tuberculosis of the prostate in the University Hospital of Pennsylvania. It appears, therefore, that the epididymis is most often the seat of the initial lesion, particularly in children.

The earliest symptom of tuberculosis of the kidney was frequency, and the next most common symptoms were burning and scalding, and hæmaturia. No doctor nowadays would wait for night sweats and hoarseness before sending sputum for bacteriological examination, but in the non-sanatorium cases the length of time that transpired before the condition was suspected was surprising—in one case as long as eighteen months, the patient being treated for a weak bladder following confinement. One feels that there should be wider recognition of the earlier symptoms of tuberculous kidney, and that all patients in whom bladder symptoms do not improve after a reasonable time should have a complete bacteriological and urological investigation.

The fallaciousness of relying on smears alone for the diagnosis of urinary tuberculosis is not so widely appreciated as one might suppose. In some of these patients with proved renal tuberculosis, the smears were negative—not once, but even twice and three times. On the contrary, guinea-pig inoculation and cultures were most reliable, and in 24 out of 26 patients with renal tuberculosis the results were positive. The two negative findings were in patients with renal occlusion where the contents of the affected kidney did not reach the bladder. Loewenstein-Jensen cultural medium was employed and positive results were obtained as early as ten days afterwards. Cultures have distinct advantages over guinea-pig inoculation. They are cheaper and easier to perform and the period of waiting is reduced by more than a half, which is most satisfactory from the patient's standpoint as well as the surgeon's. Another advantage, of course, is that only small quantities of urine are necessary for

implantation and if the inoculated guinea-pig dies of an intercurrent disease—a not uncommon happening—the whole process of ureteric catheterization has to be done all over again.

Positive findings by the laboratory are important, but of greater importance is the significance of these findings from the point of view of surgical intervention. It was not unknown some years ago for a nephrectomy to be performed simply because tubercle bacilli were found in the urine from that kidney, and great was the disappointment of the surgeon when after removal the kidney showed no evidence of tuberculous disease. The presence of tubercle bacilli in the water was then said to be due to their secretion by the kidney through damaged glomeruli.

In 1926 Medlar published post-mortem findings in 30 patients, who had been suffering from pulmonary tuberculosis. None of these patients had any symptom of renal tuberculosis and a casual examination of the kidneys revealed no gross evidence of tuberculous infection. However, as many as 100,000 slides of these kidneys were examined, and in 22 of the 30 patients evidence of tuberculosis was established. In all the patients the infection was bilateral, and in 17 there was evidence that healing had taken place. The tuberculous lesions in the kidneys were in the capillaries of the glomeruli, in the capillaries between the convoluted tubules, and in the capillaries between the connecting tubules—in that order of frequency. Lesions were also found within the lumen of the tubules, but these lesions were always associated with a lesion higher up. One can, I think, infer from Medlar's work that tuberculous lesions in the kidney can and do heal, and his work also reveals the difficulty of obtaining radiographic evidence of a tuberculous lesion when that lesion is situated in the renal parenchyma.

One now turns one's mind back to 1903, when Albarran challenged anyone to show him a patient, suffering from a tuberculous kidney, cured by means other than surgery. Medlar's work and Albarran's challenge can be reconciled and one can say that parenchymatous lesions of the kidney can heal, but that lesions which involve the calyces do not, and as a corollary to this, that pyelographic evidence of destruction of the kidney is necessary to confirm the laboratory evidence before resorting to nephrectomy.

Eight patients were sent for investigation because tubercle bacilli had been found in their urine at sanatoria or at other hospitals. This group was investigated in the

TABLE VI.—CASES WITH TUBERCULOUS BACILLURIA.

Name	Age	Sex	Disease	Laboratory findings	Investigation	Remarks
I. P.	26	F.	Tuberculosis of lungs	Tubercle in urine	Cystoscopy and pyelography negative	Cultures and guinea-pig negative.
H. L.	26	F.	Backache and debility	"	"	"
F. H.	27	F.	Pott's disease	"	Congestion of bladder—pyelography negative	Guinea-pig and culture negative.
E. N.	40	F.	Tuberculosis of lungs	"	Cystoscopy and pyelography negative	"
L. A.	32	F.	Backache, hæmaturia	"	"	"
A. J.	39	F.	Tuberculosis of lungs	"	"	"
J. M.	35	M.	"	"	"	"
E. P.	27	F.	Stone in ureter	Urine negative for tubercle	"	Culture and guinea-pig positive.
H. L.	19	F.	Backache	Tubercle in urine	"	Guinea-pig and culture negative

usual way—X-ray examination, uroselectan, cystoscopy, and pyelography. Examinations were made, for tubercle bacilli, of the total and differential urines, and the urines were cultured and implanted into guinea-pigs. In all these cases, except one, the total urine was positive for tubercle bacilli, but the guinea-pig inoculation and the cultures were negative. In the one patient with a positive guinea-pig inoculation the total urine was negative. In all cases there was no evidence on pyelography of renal damage. Five of them were suffering from active tuberculosis, four pulmonary, and one spinal, and the presence of tubercle bacilli in the urine and the absence of pyelographic evidence of tuberculosis in the renal tract can only be explained on Medlar's work. It may be argued, of course, that these acid-fast bodies were not tubercle bacilli, but other organisms, such as the smegma bacillus or acid-fast saprophytes—as demonstrated by Swabacher at the recent urological congress. In a recent paper Jeck and Handley state that the smegma bacillus is only present in urines in less than half of 1%. There is also the other fact that attention was drawn to these cases by disturbance of the urinary system, as they all had dysuria and frequency. Whatever interpretation is placed on the positive findings, the important thing is that no attempt at nephrectomy was made and these patients subsequently are all being periodically examined for tubercle bacilli in the urine. The history of one case may be instructive :—

F. H., a woman aged 27, suffering from active Pott's disease of the second lumbar vertebra, was sent to me from St. Luke's Hospital, Lowestoft, because she had frequency of micturition and tubercle bacilli had been found in the urine. *Investigation.* Uroselectan: Normal kidneys, ureters and bladder. Cystoscopy: trigone injected, orifices normal. Twenty-four hours' specimen of urine: Epithelial cells, occasional leucocytes and tubercle bacilli. Specimens from both kidneys negative for tuberculosis. Ascending pyelograms: Normal pelvic outlines. Whilst in hospital the urine was examined repeatedly and on one other occasion the urine revealed epithelial cells, leucocytes and tubercle bacilli. The patient was returned to Lowestoft for further treatment for her spine and is now free from all urinary symptoms.

Negative laboratory findings may occasionally lead to a wrong diagnosis—for example, in the condition known as renal occlusion. I use the term "renal occlusion" rather than "auto-nephrectomy." Renal occlusion is a condition in which the ureter is shut off from the bladder by obliterative ureteritis, by stricture or stone, or some extra-ureteric condition. I quote two cases showing this peculiarity :—

E. M., aged 25, was sent to hospital with a tuberculous epididymis.

History.—Urinary trouble at age of 6 years; this cleared up at the age of 8. When aged 17 fell and hurt his right hip; this did not heal. Went to hospital; diagnosis, tuberculous hip. Apart from shortening, hip condition has done well. In April 1936 developed swelling of left epididymis: sent to sanatorium, eventually sent to me for removal of the epididymis. Patient had no frequency, no burning or scalding; no hæmaturia. The epididymis was craggy and there were two sinuses in connexion with it. No tubercle bacilli found in urine either on culture or inoculation of a guinea-pig. Cystoscopy showed bladder free from cystitis, but left ureteric orifice was 1 in. behind the line of the right. No efflux from left side and ureteric catheter could not be passed. Previous uroselectan investigation had shown a normal right kidney and ureter, with no shadow on the left side, and a plain skiagram of the left kidney showed an enormous kidney tumour with calcareous deposits.

It should be said also that in the left loin there was a large palpable kidney which filled up the whole of the left side of the upper abdomen.

This was, therefore, a case of "rein mastic" with occlusion of the ureter. This patient had probably had a tuberculous kidney at the age of 6 and at the age of 8 the ureter had become occluded and the bladder symptoms abated. The kidney substance had become replaced by a mass of tuberculous caseation and he was free from all

trouble until the accident to the hip at the age of 17, so that though the symptoms had cleared up, the kidney was still a source of metastatic infection. The kidney weighed 34 oz. after removal (fig 1).



FIG. 1.—A case of "rein mastic": ureter completely occluded.

The other case was in a girl aged 15, admitted because of incontinence.

History.—At age of 2 years had had infantile paralysis; at age of 12 Pott's disease. While in a sanatorium suffered from dysuria and hæmaturia; tubercle bacilli found in urine. After two years the spinal condition healed and the urinary trouble, apart from incontinence, cleared up.

This patient had an enormous left kidney mass, which showed up well on a plain skiagram. This was therefore another case of renal occlusion with tuberculous caseation (fig. 2). Cystoscopy showed the bladder to be only slightly inflamed, and no tubercle bacilli were found on smears or after inoculation. The right ureteric orifice was normal, but the left could not be seen. This kidney weighed 28 oz. after removal.

Braasch reports that out of 621 cases of tuberculous kidney at the Mayo Clinic there were 69 with renal occlusion. The term auto-nephrectomy should only be applied to a condition in which the kidney is reduced to a small caseous sclerotic mass, and in which the chances of metastatic infection are reduced to nil and surgical interference is hardly warranted. Gibson states that this occurrence only takes place in 1% of cases. Renal occlusion as a cause of negative laboratory findings should, therefore, be borne in mind.

Uroselectan has a most favourable place as a diagnostic aid, but it should in all cases be preceded by a plain skiagram of the renal tract, as valuable information of stone and calcareous deposits can thus be obtained. Excretion urography informs



FIG. 2.—Another case of "rein mastic"



FIG. 3.—A cystogram obtained with uroselectan, showing the small contracted bladder with irregularity of the contour at the site of insertion of the left ureter.

us about the renal function and also, as a rule, indicates the diseased side. It is of distinct value in showing up renal anomalies such as double ureter, and one is reminded of the classic case of Israel in which a bifid ureter caused difficulty in diagnosis. At one time pus and tubercle bacilli were found in the specimen from the ureteric catheter and on other occasions clear urine free from tubercle bacilli. Rathbun has recently reported a further case of this nature. If the patient is instructed to hold his water as long as possible after the administration of uroselectan, the photograph of the bladder indicates the bladder capacity, and irregularities in its contour point to the diseased kidney (fig. 3). MacAlpine quotes von Lichtenberg as saying that the presence of tubercle bacilli in the urine and excretion urography with satisfactory blood chemistry are all the findings required. This is, in the main, true. Sufficient information about the other kidney may not, however, be forthcoming from the X-ray pictures, and an ascending pyelogram may be necessary to prove its soundness. One patient was admitted with a diagnosis of bilateral renal tuberculosis based solely on pathological findings and excretion urography. Excretion urography had shown a tuberculous left kidney; there was no shadow of the dye on the right side, and it was concluded that the right kidney was so diseased that it was functionless. On cystoscopy this patient was found to have advanced cystitis, but a ureteric catheter was easily passed into the right kidney. A specimen from this kidney was free from tubercle bacilli but a pyelogram revealed an extrarenal hydronephrosis. The result, of course, from the point of view of interference, was the same. It is conceivable, however, that a kidney free from tuberculosis, but with amyloid degeneration, may give a very poor shadow. Retrograde pyelography is the surest method at our disposal for proving the soundness of the opposite kidney.

There are occasions, however, when a retrograde pyelogram is impossible on either side, owing to difficulty in finding the ureteric orifices, and one must then rely on uroselectan.

For cystoscopy a low spinal anaesthetic is always employed. The information obtained by a preliminary uroselectan is useful as it gives an indication of the bladder capacity, and no attempt is made to distend the bladder more than the outlines conveyed by the cystogram. Any effort to do so will easily produce troublesome hæmorrhage. In cases of marked contraction and difficulty in obtaining a clear medium, it is wise to use an operating cystoscope. A bougie is passed first, to rule out the presence of a stricture, and the utmost gentleness is exhibited, as miliary tuberculosis is not uncommon after cystoscopy. Two deaths in this series were attributed to cystoscopy. Both patients were suffering from bilateral renal tuberculosis and the symptoms set in two days after instrumentation. These symptoms were characterized by headache, apathy and stupor, and finally coma; ocular palsies, rigidity of the neck muscles and Kernig's sign were absent. Turner reports a case of meningitis following a nephrectomy in which the symptoms are similar, and Caulk two cases following epididymectomy under local anaesthesia.

Cystoscopic findings depend on the stage of the renal lesion and the degree of secondary infection. One may find hyperæmia, tuberculous ulceration, polypoid mucous membrane, and bullous œdema. The maximum intensity of the inflammation is usually around the orifice of the affected side, but in early cases the only evidence may be redness round the ureteric orifice. The classical "golf-ball" ureteric opening was only found in this series when the disease had been present for two years or more and the most common condition of the ureteric orifice was one in which the walls were rigid and inelastic and the mouth was gaping. The bladder, however, may show no evidence of the renal condition in cases of ureteric occlusion, and a diagnosis of bilateral renal involvement should not be made on cystoscopic findings alone. The two following cases will illustrate this:—

A. X., a woman aged 40, admitted from another hospital with a diagnosis, made on cystoscopic examination, of bilateral renal tuberculosis. History of fourteen months'

frequency with burning and scalding and hæmaturia. Uroselectan showed a tuberculous left kidney and a right kidney shadow (not satisfactory owing to improper preparation). Cystoscopy: Left ureteric orifice rigid, gaping, and surrounded by tubercles. Right ureteric orifice also surrounded by tubercles, but normal in appearance.

A ureteric catheter was easily passed. Specimen taken was free from tubercle bacilli, both on smears and on guinea-pig inoculation. Pyelogram normal.

The other patient in whose case a similar diagnosis had been made was found to have advanced pulmonary tuberculosis, and double epididymitis. On cystoscopic examination no ureteric orifice could be seen, the whole bladder was covered with flakes of pus, and there was much ulceration and polypoid hypertrophy. Methylene-blue, however, gave a response on the left side in five minutes, but little or nothing on the right side in thirty. This patient was sent to a sanatorium with a view to obtaining improvement in his general condition, but he died a few weeks later, and I am indebted to Dr. Logg, Medical Superintendent of Grove Park Hospital, for the post-mortem report, which states that the right kidney was in a state of advanced tuberculosis, but that there was no evidence of tubercle on the left side.

These two cases indicate the dangers of placing too much faith on cystoscopic appearance for the diagnosis of bilateral tuberculosis.

If operation is decided upon for tuberculosis of the kidney it is important to bear in mind that it is rarely one of extreme urgency and that everything should be done to raise the patient's resistance by feeding, fresh air, and even sanatorium treatment, before submitting him to surgical intervention. These patients are not easy to handle; they require a lot of humouring, and it is advisable that they and the ward staff should be on the best of terms for some days or even weeks before operation. As in the majority of the cases there was evidence of pulmonary tuberculosis, the question of the anæsthetic was of paramount importance. In the early cases gas-and-oxygen was employed but latterly cyclopropane only has been used. Cyclopropane is not a respiratory stimulant and no chest complications follow its use; breathing is very quiet during the operation and the relaxation is sufficient. The only drawback observed was a tendency to nausea and vomiting during the first twenty-four hours.

Lett, in his Bradshaw lecture, says that he has never had reason to regret doing a nephro-ureterectomy and, in my opinion too, this is the operation of choice, and was performed in 13 of my cases. The kidney is operated on first. The patient is placed in the lateral position with the ilio-costal space made as wide as possible by elevation of the kidney bridge and by lowering the head and foot of the table. I attach great importance to this and I invariably do it myself. It saves division of the last rib and it makes easier and safer the removal of the kidney. After division of the pedicle the kidney is pushed down towards the pelvic brim and the wound is sewn up, with drainage. The patient is then placed in the Trendelenburg position and a sub-umbilical midline incision is made. The kidney is found, delivered into the wound, and given to the assistant, who holds it vertically upwards whilst the ureter is being stripped down to the bladder. The ureter is clamped flush with the bladder and divided; the cut end is sealed with pure carbolic and is embedded. The pelvic wound is also drained. In two of my cases, already mentioned, in which the kidney was very large, it was thought unwise to do the kidney part of the operation first and a uretero-nephrectomy was accordingly performed. In another case the kidney capsule was unwittingly stripped off, laying bare the kidney, with many tubercles deposited on its surface. The kidney was delivered outside the wound, and wrapped in a towel; the subumbilical stage was proceeded with, and the ureter was freed and delivered through the loin wound.

Much stress has been laid by several writers on the importance of the removal of the perinephric fat, so as to avoid contamination of the operation field and the subsequent breakdown of the wound. The perinephric fat, I think, plays very little part in this catastrophe—and it *is* a catastrophe. The causes are, I believe, rupture of the

kidney from rough handling, and contamination by the ureteric stump when the kidney only is removed. In none of my cases in which the kidney and ureter were removed together did this happen. All the loin wounds healed by first intention. There were two cases, however, in which the anterior wound broke down and this was owing, I feel, to improper sealing-off of the ureteric stump. Urologists who do not practise nephro-ureterectomy state that the ureteric stump can look after itself, but this series does not bear this out. Others, such as Marion, deliver the cut ureter into the lower part of the kidney incision for topical treatment. It is impossible to judge the condition of the lower third of the ureter from a loin incision. It is well known that the portions of the ureter more seriously involved are the upper and lower thirds. The removal of the ureter does not add more than fifteen minutes to the whole operation and it saves the patient the risk of a breakdown of his kidney wound, prolongation of his bladder symptoms, and the risk of a second operation for the removal of the ureteric stump, and also the danger of infection of the opposite kidney. In this series there were six cases in which the kidney alone was removed and, in all, the results were bad from the patient's standpoint. The history of one is interesting:—

V. S., a man aged 28, had had a right nephrectomy performed eleven months before admission. The frequency remained the same (six times at night and eight times a day). The patient had three attacks of hæmaturia, and much burning and scalding. Cystoscopy revealed an acute cystitis, the left ureteric orifice was injected but the pyelogram was normal and the specimen was negative for tubercle. The right ureteric orifice was not seen, but there were tubercles all round where it should be. Rectal examination was negative and the ureter could not be felt. It was decided that the bladder condition must be maintained by the ureter. Operation was performed and the ureter removed. Within a week of the operation the frequency had diminished and the patient is now perfectly well.

There is also a serious danger that, owing to the persistence of the bladder symptoms, an erroneous diagnosis of tuberculosis of the opposite kidney may be made. One patient, F. C., aged 28, had a right nephrectomy performed twelve months before admission to hospital, and she was admitted with the diagnosis of tuberculosis of the opposite kidney. The excretion urography showed a normal left kidney, and on cystoscopy it was possible to pass a ureteric catheter into the stump of the right ureter and to aspirate pure pus. At operation the ureteric stump was found to extend well up into the loin and was as thick as the index finger. The removal of the stump completely cured the patient of the bladder symptoms.

Four other cases in which nephrectomy alone had been performed elsewhere were admitted. In one there was a complete breakdown of the loin incision, three months after the operation. Another had multiple sinuses in the loin, which had lasted for six months. A third and fourth had tuberculosis of the other kidney and of the bladder, and both had dilated and distended ureteric stumps (fig. 4).

Another advantage in performing nephro-ureterectomy is that the vas deferens, if it has to be removed, can be followed from the internal abdominal ring to the seminal vesicle.

The exaggerated lateral position of the patient may be dangerous in cases of active Pott's disease involving the dorso-lumbar region. In one patient this complication was present, but no ill-results followed placing her in an antero-lateral position and making an oblique incision rather far forward. When there is kyphosis and marked collapse of vertebræ, the ilio-costal space may be said hardly to exist and a thoracotomy, as devised by Bernard Fey, is worth employing.

A condition which is almost as trying to the surgeon as to the patient is the treatment of tuberculous cystitis when bilateral renal tuberculosis exists, or other conditions render operation on the kidney impossible. Diathermy was most successful in one case in which there was ulceration and hypertrophy of the mucous

membrane, and in four other cases the treatment suggested by Greenberg and Brodny has been followed out. Pure methylene-blue, in 2-gr. pills, was given three times a day for three weeks and then stopped for one week as there was a tendency to diarrhoea; twice a week the bladder was washed out with distilled water and 1% methylene-blue was instilled, the patient being instructed to hold it as long as possible. The urine was made strongly alkaline, and the treatment supplemented by sunlight and infra-red rays to the hypogastrium. Methylene-blue is a weak germicide and is said to act particularly on *B. coli*, staphylococci, and streptococci; some authors state that it also has a selective action on nerve-endings and tuberculous lesions. Actually, on cystoscopy in these cases one can see the tuberculous ulcer coloured blue and the remainder of the bladder unstained. The frequency was reduced by over 50% in the patients so treated. I have no experience of other methods, such as

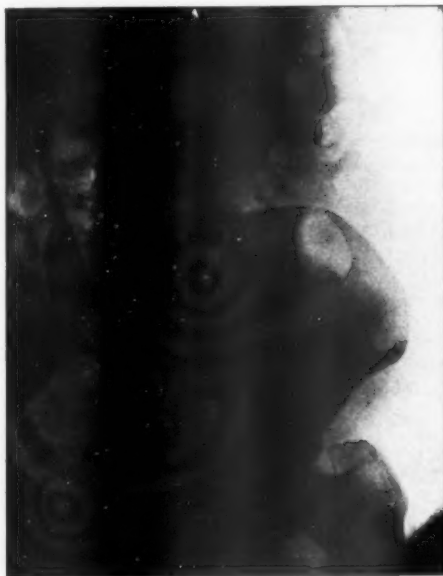


FIG. 4.—The left kidney has been removed. The ureter is dilated and tuberculous. The opposite kidney and ureter are also diseased and the bladder is small and contracted.

injections of 6% carbolic, recommended by Rovsing, or of chloride of mercury, recommended by Guyon, or of Holland's method of giving potassium iodide internally and injecting calomel emulsion in oil into the bladder. It is well known that in renal occlusion or auto-nephrectomy the bladder symptoms tend to abate, and an important suggestion has been made by Peña that diathermy to the ureteric orifice on the worse side might be useful.

In performing epididymectomy every effort should be made to preserve the testicle, especially in young people, and small abscesses in the testicle should be curetted rather than castration resorted to. Castration is, of course, necessary when the testicle is severely involved. In the presence of sinuses there is great danger of contamination of the wound and A. B. Cecil's extrusion operation is worth employing. The sinuses are treated with pure carbolic and a circular incision is made round them.

The incision is deepened and the tunica opened. The epididymis is then separated from the testicle and a pair of forceps pushed up to the external abdominal ring. The forceps are cut down upon, the vas deferens is found, and as much of it as possible is pulled through from the pelvis. It is clamped, sealed, and divided, and the distal end is delivered through the scrotal wound. Barney advises removal also of the tunica if it shows signs of disease. Ligature of the opposite vas or epididymectomy on the opposite side are drastic measures and not in keeping with the hypothesis already suggested, i.e. that epididymal infection is, as a rule, blood-borne. Bumpus and Thompson report 68 cases of genital tuberculosis and in only one was there seminal-vesicle disease. In 16 the opposite epididymis was also infected, but the seminal vesicle on that side was clear. It is a severe lowering of the patient's morale to make sterility a part of his treatment and although it is stated that 85% of these patients have azoospermia, still Bumpus and Thompson reported six cases of unilateral tuberculosis in which paternity occurred and one of a patient with bilateral tuberculous epididymis who subsequently became the father of two children. Young's operation is both severe and unnecessary, and Braasch states that the late mortality after this operation was greater than if the cases had been left alone. The operative mortality in nephrectomy is not more than 2%. In this series of three nephrectomies and 13 nephro-ureterectomies there was one death due to secondary hæmorrhage from the deep epigastric vessels. The remote results, however, tell another story. Wildbolz states that only 60%, and Barney that only 65%, are well in five years. Owing to the danger of genital involvement the prognosis is much worse in men. Westerborn states that only 40% of men are well in five years whereas 72% of women are well. Persson analysed the cause of deaths and found that 44% died from tuberculosis of the other kidney, 35.5% from tuberculosis of the lungs, and 13.3% from miliary tuberculosis. That is, a total of 93% of the deaths were due to tuberculosis.

The poor results are in great measure due to insufficient building-up of the patient's resistance after operation. He is very reluctant to undergo prolonged sanatorium treatment, especially if he has already been in a sanatorium for other forms of tuberculosis. The reluctance is due to two factors: (1) The dislike of being away from family and home, and (2) the fear of unemployment. Few employers are willing to engage a man with a tuberculous history, and patients, unless they are financially independent, cannot help being worried by this fact. The present tuberculosis scheme has done a good deal in the way of free treatment, but there seems to be a need for more settlements, such as Papworth, where the patient and his family can live in good hygienic surroundings, where the working conditions are adapted to suit his disability and where, notwithstanding this disability, he is still paid an adequate wage. No doubt the economic side of the question plays an important part in the bad results. Lett states that 80% of the well-to-do recover completely, whereas only 55% to 60% of the hospital class do so.

[I wish to record my thanks to Sir Frederick Menzies for allowing me facilities for treating these patients, to Dr. G. W. Goodhart, and Dr. I. B. Morris for carrying out the bacteriological investigations, and to Dr. W. G. Barnard for the histological work.]

BIBLIOGRAPHY

- EKEHORN, G., quoted by Davis, D. M., in article on "Tuberculosis . . . of the Kidney", *Nelson's Loose-Leaf Surgery*, 6, 651.
 THOMSON-WALKER, Sir John, "Surgical Diseases and Injuries of the Genito-urinary Organs", London, 1936.
 BARNEY, in Cabot's "Modern Urology", London, 1936.
 YOUNG, H. H. (1922). *Arch. Surg.*, 4, 334.
 SIMMONS, quoted by Barney, J. D. (1921), *Am. J. Dis. Child.*, 22, 565.
 KRAEMER, quoted by Barney, J. D. (1921), *Am. J. Dis. Child.*, 22, 565.
 KANTOROWICZ, Cabot's "Modern Urology", London, 1936.
 CUNNINGHAM, Cabot's "Modern Urology", London, 1936.
 LOWSLEY, O. S., and DUFF, J. (1930), *Ann. Surg.*, 91, 106.

- BOTHE, A. E. (1927), *J. Urol.*, **18**, 494.
 MEDLAR, E. M. (1926), *Am. J. Path.*, **2**, 291.
 ALBARRAN, J., quoted by Sir John Thomson-Walker, *loc. cit.*
 JECK, H. S., and HANDLEY (1936), *J. Urol.*, **36**, 764.
 BRAASCH, W. F. (1920), *J. A. M. A.*, **75**, 1307.
 GIBSON, T. E. (1935), *J. Urol.*, **33**, 145.
 ISRAEL, Eisendrath's "Urology", London, 1928.
 RATHBUN, Eisendrath's "Urology", London, 1928.
 MACALPINE, J. B., "Cystoscopy and Urography", Bristol, 1936.
 TURNER, J. H. (1935), *J. Urol.*, **34**, 216.
 CAULK, J. R. (1931), *J. Urol.*, **26**, 189.
 LETT, H. (1936), Bradshaw Lecture, *Lancet* (ii), 1313.
 MARION, G., "Traité d'urologie", Paris, 1921.
 FEY, B. (1925), *Bull. et mém. Soc. nat. de chir.*, **51**, 1057.
 GREENBERG, B. E., and BRODNY, M. L. (1933), *New England J. Med.*, **209**, 1153.
 PEÑA, E. de la, E., quoted by Gibson, T. E., *loc. cit.*
 CECIL, A. B. (1935), *J. Urol.*, **33**, 160.
 BUMPUS, H. C., and THOMPSON, G. J. (1928), *Surg., Gynec. and Obst.*, **47**, 791.
 WILDBOLZ, H., and VON LICHTENBERG, A., "Handbuch der Urologie", 1926.
 WESTERBORN, A., quoted by Davis, D. M., *loc. cit.*
 PERSSON, M., quoted by Davis, D. M., *loc. cit.*

Discussion.—Mr. F. E. FEILDEN: It is thought by many that a healed tuberculous focus in the kidney does not exist. This may be true. Nevertheless, eight years ago I had a patient, aged 22, who, on investigation, was found to have a definitely diseased left kidney and a grossly diseased right kidney, together with a moderate amount of bladder ulceration. Her life was a misery on account of pain and nocturnal frequency. Her weight had decreased to about 6 stones. I decided to perform right nephrectomy. When I saw the patient six months ago, she looked very fit, had no nocturnal frequency and had put on more than 3 stones in weight. All I had hoped for in operating was to give some temporary relief. I think the satisfactory result in this case is due, to a great extent, to the prolonged and careful post-operative treatment.

When the local manifestation has been removed, the importance of treating the general infection cannot be too greatly stressed. The ideal in cases of renal tuberculosis is at least six months' strict sanatorium treatment after nephrectomy.

Mr. H. P. WINSBURY-WHITE: Mr. Carver has raised a number of practical points in his interesting paper. One of the most striking facts about the complaint is the way in which the infection tends to wander casually from the genital to the urinary system and vice-versa. Caulk, of St. Louis, gave 75% as the proportion of cases of renal tuberculosis which ultimately became involved with a genital infection. It is very difficult to fit the knowledge of these facts in with the theory that the spread which takes place within these systems does so by way of the blood-stream. The explanation is, more likely, that there are easy pathways connecting the various parts of the genital and urinary tracts, along which the infection slowly travels.

Take, for example, tuberculous epididymitis. In my experience it is unusual, in cases of this condition, not to find evidence of prostatic infection. It is true that this cannot always be proved tuberculous, but in such circumstances there is high probability that it is so. Moreover why should the tuberculous process spread differently from other forms of infection? Personally I regard non-tuberculous epididymitis as secondary to a prostatic infection, and I have no recollection of any case of epididymitis which did not also yield evidence of infection in the prostate. Again, there is often a reason why this prostatic infection should attract no attention, since it is often present without producing any disturbance of micturition. Still further, if one relies on digital examination of the prostate for proof of a tuberculous infection, such a fault in technique may be responsible for an entirely wrong conclusion.

Consider a case of tuberculous epididymis on one side, characteristic to palpation, with an apparently healthy epididymis on the other side, but with definite nodules palpable on the portion of the vas deferens adjacent to the healthy epididymis. How can such a finding be explained on grounds other than the infection has made its way along the vas deferens and most likely in the outer coat?

With regard to closed renal tuberculosis, I have a vivid recollection of a post-mortem case of a man who had been killed in the street while in apparently excellent health. The left

ureteric orifice was found to be sealed-off completely—the epithelium having grown right across it—and represented on the vesical mucosa only by a dimple. The kidney was enlarged by a tuberculous cold abscess while the lumen of the ureter was completely sealed off by organized granulation tissue.

A closed condition on one side and an early infection demonstrated by intravenous urography on the other, is, in my experience, a complete justification for nephrectomy of the functionless kidney. The result in the case of a youth of 19 on whom I carried this out, convinced me of this. Nephro-ureterectomy was performed and the ureter was found to be completely occluded by caseous material. Similarly I would say that there are other bilateral cases where the disease is very advanced on one side, which is not closed, and early on the other where nephrectomy of the worse kidney is of great relief to the patient particularly with regard to bladder irritability. Such a decision can only be made as a result of intravenous pyelography. The instrumental procedure is, as a rule, highly undesirable in cases of renal tuberculosis, whereas the intravenous method is usually very satisfactory in renal tuberculosis because the subjects are often young adults, and the renal function is therefore usually excellent in at least one kidney. Often the typical picture is that of one kidney showing excavations and poor function, while the other shows perfect function, no excavations, and apparently no other deformities. In the latter circumstances the picture of the good kidney should be examined closely, for sometimes careful inspection shows that a whole, or part of, a group of minor calyces does not appear. This is likely to mean that a caseating process is going on and has not yet broken down. I do not, of course, suggest that pyelography is the sole determining factor in the diagnostic investigation. Ureteric catheterization must never be omitted. It is when this has been carried out and the disease has been definitely established on one side, while on the other, suspicion is roused by the presence of pus cells, and perhaps also of *B. coli*, tubercle bacilli not being found, that the pyelographic appearances may not be without significance. In such a case delay in carrying out nephrectomy is called for, so that perhaps in a few months, a further investigation can be made.

Mr. Carver referred to meningitis following nephrectomy. There was such a termination in one of my cases.

The problem of advising a tuberculous subject who is in doubt as to whether he should venture upon parenthood is a difficult one. I can only say that I once had a patient with renal and genital tuberculosis who entered upon this responsibility with apparent success, as he became father of a child who several years after, so far as my knowledge went, showed no evidence of tuberculosis.

Mr. HUGH LETT said that a patient with closed renal tuberculosis could not be regarded as cured, for an important focus remained whence the disease might spread to other parts of the body. Perinephric abscesses were not unknown and communication with the bladder might be re-established and the symptoms return even after the lapse of years. He considered that—with few exceptions—nephrectomy should be performed in every case, provided that the opposite kidney was healthy and there was no contra-indication to operation.

Sanatorium or similar treatment before as well as after nephrectomy was essential for certain patients. He agreed as to the dangers of immediate operation in early cases.

Mr. C. ALEX. WELLS: I agree entirely that in the early stages of renal tuberculosis the infection is often bilateral, although the development of an established lesion may take place on one side only. For the rest I will confine myself to the question of tuberculous epididymitis, on which this has some bearing.

We know from common experience that septic infection may spread along the lumen of the vas. Division of the vas in prostatic cases will prevent epididymitis occurring after operation and pus may sometimes be seen exuding from the cut end if it is left attached to the skin. On occasions when the vas is cut, urine may be seen escaping from it. From these observations it is clear that such infections spread along the lumen of the vas. It seems only logical to suppose that tuberculous infection spreads by the same route.

Given an established case of renal tuberculosis in which epididymitis develops, the only rational conclusion is that this is secondary to the kidney lesion. The fact that the opposite

epididymis is liable to become infected also, again suggests a spread along the lumen. The further fact that division of the opposite vas will prevent epididymitis on the opposite side seems to dispose of any lingering doubt on this point. In such a case there is no necessity to invoke the theory of spread by the blood-stream. Why invoke it in other cases? The pathological process applicable to the one must surely be applicable to the other.

The difficulty has arisen from the occurrence of epididymitis in patients in whom no surgical lesion is demonstrable in the kidney. The work of Medlar, Band, and others, has proved conclusively that tubercle bacilli may come through a kidney without that kidney subsequently developing a destructive surgical lesion. The lesion is microscopic and heals. This new knowledge surely explains the origin of the infection in those cases which hitherto have been supposed to be blood-borne.

Recently I have gone over the available evidence in connexion with this condition and I hope shortly to publish the text of a paper elsewhere. I feel strongly that the urinary origin of tuberculous epididymitis is the true origin and that, on this account, every case should be investigated thoroughly and repeatedly, in order that the renal lesion, if it becomes a case for surgery, should be recognized and treated as early as possible.

Section of Therapeutics and Pharmacology

President—DOROTHY C. HARE, C.B.E., M.D.

[June 8, 1937]

Hyperthyroidism and the Thyrotropic Hormone of the Hypophysis

By ARNOLD LOESER

(From the Pharmacological Institute of the University of Freiburg i. Br.)

CHANGES in thyroid function play an important role in the life of the higher animals, including man, in those adaptation processes resulting from environmental variations. In this lecture I should, however, like to draw your attention to only one aspect of thyroid dysfunction, namely hyperthyroidism.

By hyperthyroidism we understand, in general, an increase in thyroid activity, with its consequences for the organism, such as are found in Graves' disease.

Experimentally, the typical symptoms of hyperthyroidism may be produced in two ways: (1) By enteral or parenteral administration of thyroid hormone (or thyroxine). (2) By increasing the production and liberation of thyroid secretion by giving the thyrotropic hormone of the hypophysis. Of these two experimental procedures the latter approaches natural conditions more closely, since only in this way is it possible to obtain simultaneously an increased activity in the thyroid.

This paper will be concerned primarily with some of the regulatory processes in the organism during the production of hyperthyroidism with thyrotropic hormone.

The following fundamental experiment shows the existence of pituitary hyperthyroidism. When one injects a young guinea-pig with thyrotropic hormone the thyroids may be observed to be enlarged and filled with blood. Histologically, the organ shows a characteristic change, beginning in the centre of the gland and developing towards the periphery, namely, a decrease in the amount of stainable colloid, and the growth of the acinus cells which are at first cubical and then columnar, the lumen of the follicles becoming thereby smaller. These changes result in a modified picture of the gland, which resembles that of the human Basedow-thyroid, and whose intensity depends upon the amount and period of administration of the activating substance.

These changes may be observed within from thirty minutes to twelve hours after injection (Eitel and Loeser; Abelin). They are also apparent when living thyroid tissue is exposed to thyrotropic hormone, *in vitro*, in the Warburg apparatus. We may therefore conclude that the thyrotropic hormone acts directly on the gland cells, and that the nervous supply of the thyroid is of no great importance in the action of the hormone.

Similarly the thyroids of other animals may be modified by the thyrotropic hormone, the degree of change, however, depending to a considerable extent upon the species of experimental animal used.

The hormone is inactive when given by mouth. Moreover the structure of the gland is unchanged when other anterior pituitary substances are administered, e.g. the growth, or gonadotropic, hormones, when free from thyrotropic hormone. Conversely the thyrotropic hormone is without effect upon growth or upon sex glands.

These facts have been used as a basis for the biological assay of thyrotropic hormone. Junkmann and Schoeller's unit is that quantity which, injected daily for three days, causes a recognizable change in the character of the epithelium, with commencing absorption of colloid. Other units have been proposed by various investigators. Thus Rowlands and Parkes utilized the increase in weight of the thyroids as a criterion, and define as unit that total quantity of hormone which, injected in equal portions for five days, causes the weight of the thyroids of young 200-grm. guinea-pigs to be doubled (i.e. to be increased to an average of 60 mgm.). This unit is seven to thirteen times larger than that of Junkmann and Schoeller. We have used Junkmann and Schoeller's unit regularly and this is to be understood where references to units are made in this paper.

Efforts to utilize secondary functional changes resulting from the induced thyroid activity—for example, the increase in the basal metabolic rate—have not led to such satisfactory methods of assay as those already mentioned.

The following table gives some data as to the quantity present in the pituitaries of the common animals :—

TABLE I.
Thyrotropic hormone content of
anterior lobe (dry) in Junkmann-
Schoeller units per grm.

Animal			Author
Ox	...	250—500	Junkmann-Schoeller
Sheep	...	ca 1,000	Junkmann-Schoeller
Rat	...	4,000—8,000	Loeb Junkmann-Schoeller
Pig	...	300	Loeser
Horse	...	70	Loeser
Man	...	150—1,000 per grm. (in total dried gland)	Loeser <i>et Coll.</i>

It is interesting to note that the thyrotropic-hormone content of the human gland is greater in patients suffering from tuberculosis and allied chronic infections, than in patients having other pathological conditions.

That the morphological changes indicate increased thyroid activity is shown by the fact that the iodine content of the thyroid decreases, whilst that of the blood (and also of the urine) increases. The latter increase is mainly in the organically-bound iodine.

These results show quite clearly that the thyrotropic hormone not only brings about a structural change in the thyroid but also causes a liberation of iodine-containing thyroid substance from the colloid into the organism. As a result, a group of symptoms appear, already well known as a direct effect of thyroid activity, and seen in such conditions as Graves' disease.

As a primary consequence of the liberation of colloid the basal metabolic rate is raised. This rise appears in guinea-pigs as early as the first day of treatment with thyrotropic hormone, and reaches a maximum after six to ten days. The increase in the case of guinea-pigs is of the order of 26–60%, and in the case of normal rats about 26%. Similar results have been found in the human subject. These results are of additional interest, since untreated animals after hypophysectomy show an almost corresponding fall in the basal metabolic rate. Experiments to increase still further the metabolism of normal animals, by raising the hormone dosage, have been carried out unsuccessfully by various workers.

This "metabolic reaction" has been little studied in the case of pathologically changed thyroids. However, in rats with goitrous thyroids, and in humans with colloid goitre, a rapid rise in the oxygen requirement has been demonstrated. In Graves' disease the basal metabolic rate after treatment with thyrotropic hormone, rises still further (Thompson *et al.*).

A further consequence of the influence of the thyrotropic hormone on the thyroid is the change in the carbohydrate metabolism, namely, the fall in the glycogen content

of the liver. In contrast to the basal metabolic rise, the diminution of the liver glycogen occurs after about four days, just as it occurs after the administration of thyroxine, and reaches a minimum between the seventh and tenth day of treatment. The blood-sugar and the muscle glycogen are not appreciably changed under these conditions.

Of the remaining symptoms, all resulting from an increased excretion of thyroid hormone, the following may be mentioned. Increase in the excretion of water, urea, sodium chloride, and creatine, changes in the mineral metabolism, adrenal hypertrophy and a fall in the vitamin-C content of the adrenals, increased appetite, loss of hair, loss of weight, tachycardia, changes in the metabolism of the heart-muscle (Berg), and, finally, the characteristic tremor of the human subject.

These symptoms are all intimately concerned with the function of the thyroid gland; they are not observed in thyroidectomized animals. One exception appears to be the exophthalmos, which is stated to be produced in the absence of the thyroid. Marine and Rosen therefore consider that, independently of its effect upon the thyroid, the thyrotropic hormone sets up an irritation in certain centres in the mid-brain which control the sympathetic nerve to the eye, with consequent exophthalmos.

Up till now I have been chiefly concerned with the immediate but short-lived stimulation of thyroid activity by the thyrotropic hormone. Despite this immediate stimulation it has previously been found impossible to maintain the high rate of production and excretion of thyroid hormone in normal animals over long periods.

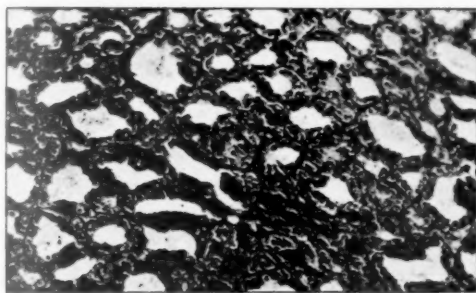


FIG. 1.—Guinea-pig's thyroid. The animal received daily for three days, 30 units of thyrotropic hormone intraperitoneally, and was killed on the fourth day. Note the growth of the epithelium, and the absence of stainable colloid. ($\times 150$.)

The maintenance of these symptoms, however, or their further development to a permanent pathological condition, becomes inhibited owing to the limited duration of the active period of the thyrotropic hormone.

This restricted effect of the hormone was noticed quite early both in animal experiments and in man. Thus Collip and Anderson found that the basal metabolism of hypophysectomized rats which, after daily injection of thyrotropic hormone had risen by 28% at the end of the first week fell, in spite of continued injection, and finally, after thirty-five days, reached a value of 29% below normal. Analogous variations, although not so marked, are observed in the carbohydrate metabolism of the liver (Loeser). In general, all the changes mentioned above—but, again, with the exception of exophthalmos—show the same marked retrogression to the normal, or subnormal condition. This is also the case with the characteristic anatomical changes found in the thyroid itself. The previously raised epithelium becomes flattened and, at the same time, the follicles of the gland become filled with stainable colloid. The gland now possesses the subnormal condition characteristic of hypophysectomized animals (figs. 1 and 2).

The impossibility of obtaining a lethal thyrotoxicosis is due to the fact that the thyroid becomes refractory to the hormone, and in spite of continued injections, not only is an increased performance on the part of the thyroid inhibited, but the initial anatomical changes in the gland retrogress, and with them all the remaining symptoms of hyperthyroidism, such as increased metabolic rate, the disappearance of liver glycogen, &c. Probably a proportion of the disappointing clinical results with thyrotropic hormone may be related to the refractory condition of the thyroid to which but little attention has been paid.

With regard to the regulatory processes in pituitary hyperthyroidism, Loeb suggested that the refractory condition of the thyroid resulted from the thyroid hormone, released in larger quantities under the influence of the thyrotropic hormone, acting back upon the thyroid, rendering it refractory to further action of the stimulator. As proof of this interpretation it was shown that simultaneous administration of thyroid substance (or thyroxine) reduced considerably the effect of the pituitary hormone (Loeb; Aron; Paal and Kleine; Loeser; Eitel, Lohr, and Loeser; Kuschinsky; Schneider and Widmann; and others). According to Kuschinsky, however, thyroxine inhibits the production and excretion of thyrotropic hormone in the hypophysis, thereby quietening the thyroid; consequently, injections of the thyrotropic hormone which would normally produce a marked effect, remain ineffective under threshold.

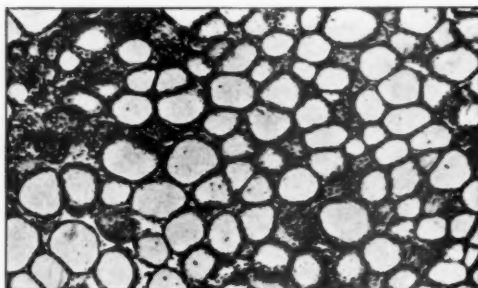


FIG. 2.—Guinea-pig's thyroid. The animal received daily, for 33 days, 30 units of thyrotropic hormone intraperitoneally, and was killed on the 34th day. Note the retrogression of the hyperplasia and the reappearance of stainable colloid. ($\times 150$.)

Nevertheless hypophysectomized animals also develop a refractory thyroid under the continued influence of thyrotropic hormone (Loeser). It follows, from this latter observation, that, in addition to the regulatory process previously outlined, there must be a second mechanism, in which the pituitary plays no part. Loeb, and also Schneider, had already considered the possibility of the presence of substances in the blood of animals injected for prolonged periods with thyrotropic hormone, which would inhibit or "neutralize" its effect. However, in their attempts to evaluate such a possibility they failed to obtain the optimum experimental conditions.

The first proof of the existence of such substances was brought forward by Collip and Anderson, who found that the blood of rats injected for many weeks with thyrotropic hormone, developed a hitherto unknown action.

Administration of this blood lowered the basal metabolic rate of normal rats and inhibited the rise in the metabolic rate caused by injection of thyrotropic hormone—but not of thyroxine. From these observations they concluded that, associated with the administration of thyrotropic hormone, a substance gradually appears in the blood, which they called an "anti-thyrotropic hormone", and which works against

the hormone. The origin, however, of this substance in the body is as yet unknown. It may be fairly definitely stated—as the result of various investigations—that it is not produced in the pituitary (Collip and Anderson; Loeser), thyroid (Eitel and Loeser), the adrenals (Scowen and Spence; Loeser and Trikojus), or the ovaries (Loeser), so that, in the interest of clarity, I prefer to use the indifferent term “antithyrotropic principle” or “antithyrotropic protective factor”.

The presence of the antithyrotropic principle may be demonstrated by using methods analogous to those involved in the determination of the thyrotropic hormone itself. One administers a known quantity of thyrotropic hormone to an experimental animal, and attempts to influence the accompanying symptoms of hyperthyroidism; e.g. the rise in the metabolic rate (Collip and Anderson), increase in weight of the thyroid (Rowlands and Parkes), or the anatomical changes in the thyroid. We usually proceed as follows: A young guinea-pig is injected, intraperitoneally, on six successive days, with equally divided portions of the active extract under investigation, and on the fifth and sixth days, in addition to the extract, known quantities of thyrotropic hormone, whereby the usual histological changes produced by the latter are suppressed (Loeser).

Using such methods, the presence of the antithyrotropic principle in the blood of rats, guinea-pigs, rabbits, dogs, sheep, and horses, after four to nine weeks' treatment with thyrotropic hormone, has been clearly demonstrated (Collip and Anderson; Eitel and Loeser; Loeser; Scowen and Spence; Rowlands and Parkes; Thompson, K. W.; Kindermann and Eichbaum).

It has also been shown that both normal animal and normal human blood have a small inhibitory action on the thyrotropic hormone (Eitel and Loeser). Such activity is, however, absent from the blood of thyroidectomized sheep (Eitel and Loeser), and could not be demonstrated in the serum of patients with exophthalmic goitre (Scowen and Spence; Herold).

The degree of inhibition shown by normal blood varies markedly in different species and is not always constant in any particular species. The following data will give some idea of the extent of the inhibition obtained with sheep's blood: 12 c.c. of the serum from a sheep which had been treated for several weeks with thyrotropic hormone (1,700 units per week), suppressed the thyroid action of 40–60 units of thyrotropic hormone in the guinea-pig, whereas 12 c.c. of mixed normal sheep blood only protected against 10 units of the hormone (Eitel and Loeser).

A similar activity is, moreover, exhibited by blood fractions obtained from normal sheep blood or serum by chemical processes. Trikojus and I have succeeded, by suitable adsorption and elution methods, in concentrating the antithyrotropic principle, and in obtaining stable powders, a total of 25 mgm. of which suppresses the action of at least 10 units of thyrotropic hormone. Such extracts are also active when given by mouth. The dried extracts were obtained by first precipitating most of the proteins from sheep serum with a suitable concentration of alkaline acetone, and then by quantitatively adsorbing the active principle from the liquor with benzoic acid. It is of additional interest that, although the inhibitory effect of organically bound iodine is well known, our dried active extracts contain but a minute quantity of this element, e.g. 2.5% per gram.

The action of the inhibitory factor is not restricted to one type of specific immunity reaction, since it is possible, with a thyrotropic hormone obtained from a species A (cattle), to produce in a second species B (sheep), factors which suppress in a guinea-pig the activity of a thyrotropic hormone obtained from a third species C (pig) (Loeser, A., and Thompson, K. W.). Then it is known that after a certain latent period the inhibitory action of normal blood may be increased by the continued administration of thyrotropic hormone (Loeser, *et al.*). This increase, moreover, is only possible in the presence of the thyroid, and cannot be obtained in thyroidectomized animals. In the latter case, however, the simultaneous administration of thyroxine

will bring about the desired result. Inorganic iodine is, in this connexion, without effect (Eitel and Loeser).

The antithyrotropic principle is hormone-specific, since it is only antagonistic towards the thyrotropic hormone. Moreover, even though the quantity present in the blood may be increased by the administration of thyroxine, it does not possess an action against the effect of thyroid hormone or thyroxine (Collip and Anderson; Eitel and Loeser; Grab).

One is thus led to consider that the development of refractoriness in the thyroid, in pituitary hyperthyroidism, is an adaptive process, by means of which the organism protects the thyroid against the thyrotropic hormone of the pars anterior. This protective effect, as I have already indicated, may result either from a limitation of the hormone production and its excretion from the pituitary, or from a protection of the thyroid from the potential effect of the thyrotropic hormone. The net result is, in both cases, the same: the activity of the thyroid is suppressed, and the over-excretion of thyroid hormone into the organism does not occur: in other words the condition of hyperthyroidism is not produced.

Experimentally, both these ways are feasible. The excretion of hormone from the pituitary can be limited by the administration of thyroxine. The protection of the thyroid may be achieved through a substance, or substances, normally present in blood, an antithyrotropic principle, the amount of which may be increased when the organism is made hyperthyroid by thyrotropic hormone, thyroid hormone, or thyroxine. This antithyrotropic factor appears to act directly on the thyroid, so that the latter becomes less sensitive to stimulating influences. Thereby, the further excretion of thyroid hormone from the hyperfunctioning gland is restricted, and the organism protected from a flooding with thyroid secretion. Thus the thyrotropic hormone not only possesses the property of activating the thyroid gland but, owing to the enhancement of the latter's function, brings into being counter-regulatory processes which protect the organ against all further stimulation from the pituitary hormone, and eventually reproduce the original state of the gland.

In spite, however, of the organism's dual capacity of safeguarding itself against the condition of hyperthyroidism, the protection of the thyroid against the action of the thyrotropic hormone is not absolute. The refractory condition of the thyroid, which, after a certain latent period, results from the administration of the pituitary hormone, or of thyroxine, can in fact be broken through if one administers the pituitary hormone in progressively increasing amounts, i.e. sufficient to over-ride the effect of the gradually developing protection. I have recently found (Loeser) that, by this means, the anatomical and functional symptoms of hyperthyroidism may be not only maintained, but progressively increased, until death finally supervenes.

The oxygen requirement in the case of two groups of four guinea-pigs was measured. In the first group each animal received (intraperitoneally) a daily quantity of hormone, which remained constant for three days, and was then doubled for the next three days, and so on. The initial dosage was 20 units and the final dosage 400 units. The total amount administered being 1,700 units, when death intervened. In the second group, each animal received the same total quantity (1,700 units), equally divided in doses of 120 units.

Let us now consider the course of the hyperthyroidism in the first group:—

The oxygen requirement, after the daily administration of 20 units, rose without a pronounced latent period. This rise continued parallel to the increase in dosage so that the oxygen requirement on the ninth day reached an average of 70% (56–82%) above the normal. The metabolism of two animals of this group decreased somewhat before death, whereas in the case of the other two the rise was maintained until the end. The greatly increased oxygen requirement exercised no corresponding influence on the body-weight.

The thyroids of all the animals in this group were greatly enlarged, and showed,

on the average, a fivefold weight increase compared with the normal weight, which, according to Rowlands and Parkes may be taken as about 31 mgm. for 200-grm. guinea-pigs. A similar hypertrophy was also present in the adrenals which showed an increase of 140%, taking 100 mgm. as the average weights for normal guinea-pigs of 200 grm. (Loeser).

Finally, a hitherto unobserved action of thyrotropic hormone was observed, namely the production of fatty degeneration and diffuse necrosis in the liver and kidneys. These effects, which are only observed under the condition of a progressively increasing hormone dosage, would indicate a pronounced thyrotoxicosis since they are also a feature of Graves' disease.

In the case of the animals in the second group, in which a *constant* hormone dosage was maintained—120 units per day—the oxygen requirement also rose rapidly but reached a maximum between the seventh and ninth day. The rise was thus only temporary. Further, the oxygen values showed noticeable irregularities which, I think, are due to the functioning of the counter-regulatory processes, in contrast to the apparent lack of inhibition in the hyperthyroid state induced by progressively increasing dosage.

In comparison with the first group, the highest value of the oxygen requirement corresponds to a rise of 29–40% (average 35%), in spite of the fact that in this period more than double the quantity of hormone had been administered to this second group.

The weight of the thyroids only increased threefold. In contrast to the thyroids of the animals in the first group, those of the second group have, in places, considerable quantities of colloid. It is, however, impossible to say whether this represents colloid not yet adsorbed, or whether, as a result of a counter-regulation, there is already a formation of new colloid.

From the above results it seems obvious that the duration of the effect of the thyrotropic hormone may be extended by continually raising the dosage. Where this is done the animals, in contrast to those receiving a constant dosage, may be maintained in a state of hyperthyroidism until death intervenes.

The extended period of action of the thyrotropic hormone with progressively increasing dosage is also closely related to the modified type of metabolism. Whilst the oxygen requirement with constant dosage reaches a maximum, after a short time, and then soon begins to fall, the increase in the oxygen requirement, with progressively increasing dosage, continues until the death of the animals.

All these observations lead to the conclusion that, by continually increasing the hormone dosage, it is possible to break through all the safeguards which protect the thyroid against the thyrotropic hormone, and therefore the organism from a flooding with thyroid secretion.

The refractory condition of the thyroid—and here I return to the original point under discussion—which with *constant* dosage of pituitary hormone sets in rather rapidly, may be over-ridden by continually raising the dosage. In my opinion, therefore, at least two ways are conceivable for the production of a continual state of hyperthyroidism: Firstly, by a continual animation of thyroid activity with the normal protective function of the organism (i.e. the conditions for the production of the antithyrotropic principle) still preserved, namely, the consequence of a real pituitary hyperthyroidism; secondly, the failure of the protective function, accompanied by a constant or increasing animation of thyroid activity. With these conceptions the condition of experimental hyperthyroidism and its related clinical counterpart—Graves' disease, take on a new aspect, and with it the possibility of a causal therapy, as, for example, the administration of a highly active anti-thyrotropic factor worthy of consideration in certain cases.

In this paper I have attempted to show the importance of the thyrotropic hormone in the production of experimental hyperthyroidism, to review the interplay of the

various regulating factors in the organism—as they appear from the experimental observations—and to indicate how far these results bear upon the pathogenesis of hyperthyroidism and, in particular, of Graves' disease.

In conclusion, I should like to acknowledge my indebtedness to my friend, Dr. V. M. Trikojus, of the University of Sydney, who has kindly carried out the English translation.

BIBLIOGRAPHY

- ABELIN, *Wien. klin. Wchnschr.*, 1936, **49**, 1185.
 BERG, *Arch. f. exper. Path. u. Pharmacol.*, 1937, **185**, 359.
 COLLIP and ANDERSON *J. Physiol.*, 1934, **82**, 11; *Lancet*, 1934 (i), **76**, 784.
 EITEL and LOESER, *Arch. f. exper. Path. u. Pharmacol.*, 1932, **167**, 381; 1935, **177**, 739; **179**, 441; *Klin. Wchnschr.*, 1934, **13** (ii), 1677.
 EITEL, LÖHR, and LOESER, *Arch. f. Exp. Path.*, 1935, **177**, 743.
 GRAB, *Chemie und Medizin III*, 1936, p. 214.
 HEROLD, *Klin. Wchnschr.*, 1934, **13** (ii), 1242.
 JUNKMANN und SCHOELLER, *Klin. Wchnschr.*, 1932, **11** (ii), 1176.
 KINDERMANN and EICHBAUM, *Klin. Wchnschr.*, 1937, **16**, 430.
 KUSCHINSKY, *Arch. f. exper. Path. u. Pharmacol.*, 1933, **170**, 520.
 LOEB, *Klin. Wchnschr.*, 1932, **11** (ii), 2121, 2156.
 LOEB, BASSETT, and FRIEDMANN, *Endocrinology*, 1935, **19**, 330; *Klin. Wchnschr.*, 1932, **11** (ii), 2121, 2156.
 LOESER, *Arch. f. exper. Path. u. Pharmacol.*, 1933, **173**, 62; 1934, **176**, 697; 1936, **184**, 23; *Zentralbl. f. inn. Med.*, 1936, **27**, 569.
 LOESER and TRIKOJUS, *Arch. f. exper. Path. u. Pharmacol.*, 1937, **185**, 232; *Klin. Wchnschr.*, 1937, **16**, 313.
 MARINE and ROSEN, *Proc. Soc. Exper. Biol. and Med.*, 1933, **30**, 901.
 MÜLLER, EITEL, LOESER, *Arch. f. exper. Path. u. Pharmacol.*, 1935, **179**, 427.
 OEHRME, *Arch. f. exper. Path. u. Pharmacol.*, 1937, **184**, 558, 573; *Klin. Wchnschr.*, 1936, **15** (i), 512.
 ROWLANDS and PARKES, *Biochem. J.*, 1934, **28**, 1829; *J. Physiol.*, 1936, **88**, 298; *Proc. Roy. Soc. London*, 1936, **120**, 114.
 SCHITTENHELM und EISLER, *Ztschr. f. d. ges. exper. Med.*, 1935, **95**, 122.
 SCHNEIDER, *Deutsche Ztschr. f. Chir.*, 1934, **242**, 187.
 SCHNEIDER und WIDMANN, *Deutsche Ztschr. f. Chir.*, 1933, **241**, 15, 78.
 SCHOEDER, *Arch. f. exper. Path. u. Pharmacol.*, 1933, **173**, 326.
 SCOWEN and SPENCE, *J. Physiol.*, 1936, **86**, 112.
 THOMPSON, K. W., *Proc. Soc. Exper. Biol. and Med.*, 1937, **35**, 637.
 THOMPSON, W. O., THOMPSON, P. K., and TAYLOR, D., *West. J. Surg.*, 1936, **44**, 507.

Section of Comparative Medicine

President—GEORGE W. DUNKIN, M.R.C.V.S.

[May 26, 1937]

A Few Remarks on Snake Venom, Its Source, Method of Collection and Uses

(Introducing the author's coloured cinematograph film of Brazilian snakes)

By Sir WELDON DALRYMPLE-CHAMPNEYS, Bt., M.D., F.R.C.P.

It is quite impossible here to give more than the slightest outline of a subject so complicated as that of snake venom. Dr. Burgess Barnett (Curator of Reptiles to the Zoological Society of London) and myself have a great deal of valuable information on this subject which we hope one day to sort out and arrange, but to-day I must be content to try to excite your interest in a branch of scientific research which I believe will be of great importance in the future.

It has always seemed to me possible that the ancient Greeks may have kept snakes in the temples of Æsculapius for other purposes than what we should nowadays call "atmosphere", and that the nightly visitations of these reptiles to the patients undergoing a cure may have been permitted on account of the benefit found to result sometimes from their bites. However this may be, it is certain that accidental snake-bite has led in recent years to important discoveries in the treatment of disease, for instance the treatment of epilepsy by the venom of the puff-adder.

The venom of any species of snake was formerly regarded as a single chemical substance, but as the result of work done in India, Brazil, and elsewhere, we now know that not only do different venoms differ greatly from each other, but that each individual venom contains a number of constituents, each with a specific action of its own. As long ago as 1904 Elliot showed that the venom of the common Indian cobra has a strong vasoconstrictor action as well as a neurotoxic one. Neurotoxin is one of the most important constituents of snake venoms, because of its lethal effect and its therapeutic value, but different venoms differ greatly in their neurotoxin content, one of the richest in this constituent being that of *Échis carinata*, a viper found in India, Arabia, Persia, and North Africa. The venom of the only other member of the viper family found in India, viz. Russell's viper, has an even higher neurotoxin content, and this venom is also remarkable for its powerful coagulant action on blood. The venom of the rattlesnakes (belonging to the family of Crotalidae or "pit-vipers") is much poorer in neurotoxin and coagulant than that of Russell's viper, and the venom of the American "water-mocassin" (*Agkistrodon piscivorus*), a member of the same family, contains a definite anti-coagulant. Cobra venom has a very powerful—and very valuable—analgesic action, but whether this is due to the same neurotoxic constituent which causes respiratory paralysis, and which according to Ganguly and Malkana is a secondary protease, is still uncertain. The proteolytic action of cobra venom and its effect on tissue growth have also received attention lately and may prove to be of importance in the treatment of malignant new growths.

The principal poisonous snakes of Brazil are the "coral snakes", belonging to the genus *Micrurus* of the family Elapidae, the South American "rattlesnake" (*Crotalus terrificus*), the rare but extremely dangerous "bushmaster" (*Lachesis muta*), and the various "fer-de-lance" (*Bothrops*), the three latter belonging to the family Crotalidae or "pit-vipers". The beautiful coral snakes of South America are extremely poisonous, but are closely imitated by the harmless "false coral snakes", *Erythrolamprus æsculapii* of Brazil and *Cemophora coccinea* of the South-eastern United States. The true coral snake has a peculiar mode of attack, turning and "snapping" in all directions, instead of "striking". Two specimens of a very beautiful species of coral snake, *Micrurus frontalis*, were among the species which I succeeded in bringing to this country alive for the first time on record.

The bushmaster is an especially terrible snake, not only on account of its size (it sometimes attains a length of 12 ft.), the great length of its fangs, and the deadliness of its poison, but also because it shares with the black and green mambas of Africa and the hamadryas or "king-cobra" of India the grim distinction of being the only poisonous snakes which attack man quite unprovoked.

A very large number of snakes belonging to the *Opisthoglyphæ*, or back-fanged snakes, which were formerly regarded as harmless, are now known to be poisonous. The fangs of these snakes are furrowed or grooved instead of canaliculated, and to inject the venom into their victim they must advance their jaws in a series of chewing movements, instead of "striking" and withdrawing as do the Elapidae and Viperidae. The coral snake, as already mentioned, twists and snaps from side to side, whilst the "Ringhals cobra" (*Sepeidon hamachates*) ejects jets of venom for six to eight feet in front of it. In fact the modes of attack of different poisonous snakes present an almost endless variety, and anyone thinking of collecting them will do well to study their tricks, as safety will often depend upon such knowledge.

The film which I am going to show gives a clear picture of the method of catching snakes and packing them for transport, but a word or two of explanation may help. The *safest* way of capturing a snake and the one nearly always employed in "zoos", where the escape of a specimen might be a serious matter, is by means of a "lasso" or "noose" consisting of a flat leather strap fastened to the end of a pole about 5 ft. in length. This strap or thong is slipped over the head of the snake and tightened round the neck by pulling on a wire or string led up to the top of the pole. The *easiest* way of catching a snake is, however, to pick it up on a crook and pop it quickly into a bag or box, but if it is necessary to handle the snakes for the purposes of "milking" (i.e. the extraction of the venom), or examination, the noose is nearly always used.

The therapeutic possibilities of snake-venom are, I believe, only just beginning to be explored, but the results already obtained are of considerable importance. The best known of these uses is, perhaps, the control of bleeding in such conditions as hæmophilia, purpura hæmorrhagica, bleeding from the gums following tooth extraction, epistaxis, hæmoptysis, &c. For this purpose the venom of Russell's viper (also known as the "daboia" or "tic polonga") is chiefly used owing to its high content of blood coagulant, but the venom of the American "water moccasin" (*Agkistrodon piscivorus*) is also used for this purpose. I have already referred to the accidental discovery of the value of puff-adder venom in the treatment of epilepsy. An epileptic had the good luck to be bitten, and since then the venom has been used on many other patients and this venom and cobra venom are at present being tried out in this country by Burgess Barnett. The results so far obtained fully justify a continued trial of this method. Another very promising line of treatment is the relief of pain by means of cobra venom. Burgess Barnett and I, and other workers both here and abroad, have obtained very good results in the treatment of pain in such varied conditions as inoperable carcinoma, chronic osteoarthritis, tabes dorsalis, &c.

Snake-bite is not a very serious danger here, but in Brazil, and other countries where poisonous snakes swarm, the protection of the human population is a matter of great importance, and it has fortunately been found possible to prepare protective serum or "antivenin" against most varieties of poisonous snakes.

At the Butantan Institute, São Paulo, Brazil, the Director of which is Dr. do Amoral, where about 1,500 snakes are milked every month, large quantities of protective sera are prepared from horses and distributed in return for poisonous snakes sent from the interior.

Cutaneous Streptothricosis: A Case in Great Britain

By A. W. STABLEFORTH

(Department of Preventive Medicine, Royal Veterinary College, London)

THE case is of interest because, so far as I am aware, no similar case has previously been reported in this country. The subject was a horse aged about 16 years, which entered the Serum Department of the Lister Institute (Elstree) in September 1936. Immunization with killed suspensions of *C. diphtheriae* was begun on November 3, 1936 and continued until January 28, 1937. I am indebted to Dr. G. F. Petrie for drawing my attention to the lesions present in this case and for data regarding its history and certain examinations prior to February 1937.

Lesions first appeared early in January 1937 and, with minor variations, continued to spread from their edges and to appear at other places until the middle of March. Up to this point, cultures were obtained with relative ease. At this time the horse had lost much in general condition, and an increased corn-ration was fed. Marked improvement followed and, with minor set-backs, continued until the end of June, when the horse was killed; the existent lesions had then healed and new ones ceased to appear. Treatment was not carried out, on account of the spontaneous improvement. Nine different samples of material were examined during the last month, including some from small lesions of a different clinical nature, which had developed later. The results were entirely negative, contrasting strongly with the relative ease with which cultures had been obtained earlier. Material was examined for evidence of ringworm and for acari on four occasions from January to June, always with a negative result.

Typical lesions are shown in the photograph which were taken at the end of March (fig. 1). The earliest lesion consisted of a slightly raised roundish area a little over half a centimetre in diameter, on which the hairs were raised, giving an appearance like the head of a small paint-brush. These tufts could easily be removed, bringing with them the epidermis and leaving a greyish, shining, moist, and slightly cupped area without obvious pus. More advanced lesions were up to 2 cm. in diameter and deeper, and when they were removed a thin layer of pus was disclosed. If the early lesion was removed, a secondary one, covered by a scab, often developed underneath. Lesions at times became confluent. They were confined to the upper layers of the skin and the hair follicles.

Smears from the lesions showed small numbers of organisms arranged singly or, more often, apparently in chains, resembling at first sight chains of heavily encapsulated streptococci. Closer examination showed, however, that these were not streptococci but filaments across which were laid deeply Gram-positive oval elements, sometimes of a dumb-bell shape.

Cultures were easily obtained on serum-agar or blood-agar, or in serum-broth. On serum-agar a heavy shining pale orange-yellow growth was usually produced, which resembled that of a staphylococcus, except that it was at times of very tough

consistence and firmly adherent to the medium. At other times the growth was thinner and greyish, with small, pale-pigmented raised areas. In blood-agar deep colonies produced β -hæmolysis or sometimes a hazy type like that which may be produced by *Staphylococcus aureus*. Colonies increased in size for four days, deep colonies being then up to 2 mm. in diameter and having a markedly fuzzy edge. In serum broth growths occurred in small rounded colonies at the bottom or were attached to the glass at the sides. Growth, on all media, was relatively slow and reached its maximum at three to four days. The fermentation reactions were those of the organism isolated from similar lesions in other countries (see following paper by J. R. Hudson, p. 57).

The morphology in culture varied greatly, particularly with age, and a full description cannot be given here. Some of the characteristic features are shown in the



FIG. 1.

photographs (figs. 2 and 3). With pure cultures, there have been seen plain single homogeneously staining filaments, "barred" filaments, multiple filaments or "fingers", and free coccoid elements. One or other form was often predominant. The plain filament is not strongly Gram-positive and does not stain deeply with the usual aniline dyes. As it develops, the older end becomes "barred" and definite oval elements appear in the filament. These stain deeply, are strongly Gram-positive and are laid transversely. They appear to extend laterally until each oval element has a dumb-bell appearance and the older end of the filament appears double. The process may continue until a "finger" is produced having at its growing end a single homogeneously staining filament and at its older end a quadruple filament. At this stage, or earlier, the filament appears to break up transversely. In some observations, made with a warm cabinet (see Hudson, p. 57) the growth of the filaments and subsequent break-up was watched, the double filament breaking eventually into packets each containing four to sixteen coccoid elements. Continued observation of these packets was difficult and further break-up or development of the coccoid elements was not followed up. Appearances strongly suggesting that a filamentous outgrowth from the coccoid elements occurs were seen in stained and unstained preparations. In addition to the forms described, much larger coccoid elements,

arranged singly or in clumps, were at times seen, but it was not possible to decide whether they were part of the normal life-cycle, or degenerate forms.

Rabbits were inoculated with a suspension of triturated material or culture rubbed into the skin of the abdomen, from which the hair had been plucked. After twenty-four hours, the whole area was covered with whitish pustules up to 2 mm. in diameter, and the organism was recovered from these, though with difficulty. After forty-eight hours the lesions had begun to regress but had coalesced in parts where the inoculum was heavy. By the third or fourth day a scab had formed, a part of which had often already fallen off. The lesions described were not produced by similar treatment of rabbits with material from horses affected with skin lesions of other nature. They were also quite different from the typical lesions produced by the streptothrix from bovines or sheep in Kenya from the fourth to the sixth day onwards (*see* Hudson, p. 57).



FIG. 2 $\times 450$.



FIG. 3. $\times 1,000$.

Rabbits which had been treated with material from the cases described and had recovered, were inoculated about a month later with cultures, isolated by Hudson, from typical cases of streptothricosis in Kenya, and they developed typical lesions of that condition. No evidence of cross-immunity was present. Vice versa, animals treated with culture from the Kenya condition, which had recovered, were inoculated with culture from the case described and developed the twenty-four to forty-eight hour pustules characteristic of this organism.

The organism recovered from the case described is closely related to those isolated from cases of cutaneous streptothricosis in Africa and from "lumpy wool" in Australia, being similar culturally and in its various morphological characters, but producing a different and characteristic lesion in artificially inoculated rabbits.

Cutaneous Streptothricosis

By J. R. HUDSON

(Division of Veterinary Research, Kabete, Kenya Colony)

STREPTOTHRICOSIS has been recognized for about twenty years in British tropical African colonies as a clinical entity. Van Saceghem (1915) described the lesions of the disease, called by him "dermatose contagieuse" or "impetigo contagieux", and also the associated organism, which he named *Dermatophilus congolensis*. In Northern Rhodesia the disease is also called "Senkobo scab".

Description of the lesions.—The disease affects, naturally, cattle, sheep, goats, and horses.

In cattle the lesions may be localized or spread over much of the skin surface. Local lesions tend to spread when the condition of the animal is lowered, as by rinderpest (Hornby, 1934), or during the rainy season, when the wet coat and warm climate unite to favour growth of the causal organism. The local lesion appears as a collection of hairs matted together and forming a bundle like a damp camel-hair paint-brush. These bundles, which vary from a few hairs up to 10 mm. in diameter, project above the general surface of the coat. When pulled, they are easily detached and leave a moist greyish patch on the skin and a thin concave moist crust at the base of the bundle. Isolated lesions are most often observed on the side of the neck, but may occur on any part of the body or head. When the lesions are more generalized, larger patches up to several centimetres in diameter are found, and hair is often lost from parts of these. There is little or no pruritus at any stage of the disease.

In Merino-grade sheep, the most characteristic sites for the lesions are the lips, ears, and coronets. Around the mouth the lesions are usually isolated, consisting of hard pencils of matted hairs varying in diameter up to 6 or 7 mm., and resemble closely the isolated lesions found in cattle. On the ears, where the hair is normally short, the lesions produced are broader, flatter, and more scabby. Lesions in the fleece are very rare and only thin scabs along the centre of the back have been encountered.

Goats are not often affected by the disease in Kenya. Beaton (1932) has described it in goats in Nigeria and states that it is chronic during the dry weather and that during the rainy season it spreads over the body surface, including the lower aspect of the abdomen and the inner surface of the forelegs and thighs.

In horses, the lesions are strictly comparable with those seen in cattle, but the disease is not as common among horses in Kenya as was at one time supposed. Streptothricosis has been confused with a similar condition of undetermined aetiology, both being referred to as "Uasin Gishu skin disease".

In all the species in which streptothricosis occurs naturally, it appears as a chronic condition. In certain circumstances, not all of which are known, the disease passes from the isolated-lesion phase to a severe eruption covering much of the body surface. As conditions become less favourable to the disease, animals, unless very severely affected, either recover completely or show a return to the chronic state in which only a few isolated lesions are present. Even a severe attack of the disease does not appear to produce any immunity.

Appearance of the organism in lesions.—Smears from the moist area left when a scab has been removed, or from the concave surface at the base of a "pencil", show abundant mycelia, epidermal cells, and leucocytes. The mycelium consists of branching filaments, composed of rows of Gram-positive coccoid-elements united in a homogeneous matrix. Although the filaments are commonly 2 to 4 coccoid-elements wide, they may occasionally be 8 elements in width. In addition, isolated and tetrad forms are found.

Cultivation.—The organism grows on the surface of blood- or serum-agar or in serum-broth, and also in poured blood-agar plates, where deeper colonies produce a more marked hæmolytic than surface ones. Growth on plain- or glucose-agar is meagre and no growth occurs under anaerobic conditions. The optimum temperature is about 37.5° C.

On the surface of blood- or serum-agar the growth varies and may be white, creamy-buff, or golden. The usual form is a semi-shiny, continuous, flat, creamy-buff streak with local thickenings appearing as smooth golden ridges or spots. Low cones of growth, the surface broken by rough, radiating ridges of varying length, also occur frequently. This type of growth is leathery in consistence and may be white or golden. A third variant consists of isolated colonies having a flat surface slightly above the

surface of the medium, and feathery processes of different lengths which project down into the medium. These variations are usually only temporary, and change to another type often occurs suddenly.

In serum-broth the most frequent type of growth consists of small furry balls at the bottom of the tube. Sometimes, however, a slimy scum appears on the surface and, if tubes are incubated in an oblique position, the sides which have been underneath may be covered with a fine growth giving an appearance like frosted glass. Diffuse clouding of the medium is not usual, but has been observed on one or two occasions.

In poured blood-agar plates colonies have a radiating filamentous appearance; some are compact and dense, others loose and more transparent.

The organism produces acid in glucose and laevulose after two to three days' incubation and a low degree of acidity in glycerine after ten to fourteen days. No acid is produced in lactose, saccharose, mannite, dulcitol, arabinose, raffinose, rhamnose, salicin, sorbite, xylose, inulin, or inositol. The methyl-red and Voges-Proskauer tests are negative.

Appearance of the organism in cultures.—The appearance of the organism in smears and impressions varies with the age of the culture and with the strain, and the records are based on preparations from cultures of different ages and observations made with a warm cabinet (37° C.). All cultures at some early stage show the presence of solid, branching, Gram-positive filaments, which later develop into chains of either round or oval coccoid elements in a zoogloeal matrix. Each oval element has its long axis situated across the filament and elongates to produce a transverse bar, which becomes dumb-bell shaped and then divides into two coccoid-elements. Filaments of more than two elements in width have not been observed in the process of formation, but are found in smears. In old cultures the coccoid elements break up into packets and pairs.

In some cultures complete development is more rapid than in others, and a smear made after twenty-four hours' incubation reveals hardly any filaments, but packets of coccoid elements with short triangular processes. At the apex of some of them a short solid rod can be demonstrated. It appears that in these cultures the solid filament develops into the later forms almost as rapidly as it is produced. Although it is of course possible that some of the coccoid elements multiply and produce further elements, such a method of reproduction has not been observed in hanging-drop preparations.

In recent observations filaments have been demonstrated in young cultures without difficulty, although Van Saceghem (1934) had not been able to find filamentous forms in cultures. The organism is therefore more likely to belong to the genus *Actinomyces* than to be an aberrant coccus.

Pathogenicity.—The organism is non-pathogenic when inoculated intraperitoneally, or intravenously, into rabbits, guinea-pigs, rats, or mice. When cultures of strains from Kenya are rubbed on the skin of a rabbit from which the hair has been plucked, a typical train of changes is produced. Slight erythema occurs after twenty-four hours, and increases in intensity, and the skin becomes tumified. Fine, shiny points of scab appear about the fourth day and increase in number and extent until the whole area is covered with a thin, dry scab. As the scab becomes thicker, swelling of the skin decreases. The scab falls between the ninth and thirteenth day and leaves the skin clean and healthy in appearance, and a new growth of hair soon covers the inoculated area. The organism is easily recovered from the scab, especially if the scab is placed in a desiccator over strong sulphuric acid for nine days, as this procedure kills most contaminating organisms.

If a good reaction of moderate extent has occurred, a rabbit usually proves refractory to a second application of culture, but if the reaction has been less marked, immunity may be restricted to the site of the original inoculation. By this method

bovine and ovine strains from Kenya have been shown to give cross-protection against each other.

Scarification with the organism on the inner surface of the thigh of lambs, sheep, and calves, produces a mild transient lesion only. The scab is usually scanty, although the organism can be recovered from it.

Microscopic examination of sections of the affected skin of sheep and rabbits shows that the organism multiplies within the hair follicles and on the moist surface of the skin. At no time has it been found below the epidermal layers.

Relation of the condition to lumpy wool.—In 1929 Bull described a condition in Australia known as lumpy wool or mycotic dermatitis. This is a disease of sheep, clinically similar to streptothricosis, but differing in that the organism attacks the follicles of the fleece rather than those of the hairy parts. The exudate mats the wool and as the wool pushes up, a dense horny "growth" is produced. This "growth" is often several inches in diameter at the base and varies in height with the length of the staple. The "growth" has a concave base like the pencil in streptothricosis, and as it causes no inconvenience to the sheep is rarely noticed except at shearing time. Lumpy wool occurs in Australia and S. Africa, and in both countries occasional cases are seen in which the mouth and ears are affected with lesions identical with those of streptothricosis. Smears from the base of a lumpy wool "growth" show branching mycelia of solid Gram-positive filaments identical with those seen in early cultures of the organism of streptothricosis; moreover, in cultures of more than twenty-four hours' growth of the lumpy wool organism, *Actinomyces dermatonomus* (Bull), filaments composed of rows of coccoid elements are present. The two organisms have also similar biochemical characters and produce similar lesions on the skin of rabbits.

Attempts to produce lumpy wool in sheep in Kenya, by pouring cultures on the fleece and by inoculating the skin of the back by scarification have, however, been unsuccessful even when culture has been applied repeatedly, and the site of inoculation kept moist by pads of cotton-wool soaked with water daily.

Albiston (1933) has reported a case of lumpy wool in a calf in Australia. The description of the lesions resembles that of the lesions of cutaneous streptothricosis and a similar, if not identical, organism was isolated.

There can be little doubt that the two organisms, that of lumpy wool and that of cutaneous streptothricosis, are very closely related. The former has been placed by Bull in the genus *Actinomyces* and the tentative suggestion is made that the latter be called *Actinomyces congolensis*.

Thanks are due to Mr. R. Daubney, Chief Veterinary Research Officer, Kenya Colony, for permission to present this note, and to Professor Minett and Dr. Stableforth of the Royal Veterinary College, London, for facilities to continue the studies on this subject.

REFERENCES

- ALBISTON, H. E. (1933), *Australian Vet. J.*, **9**, 107.
BEATON, W. G., Annual Report of the Veterinary Department, Nigeria, for 1932, p. 20.
BULL, L. B. (1929), *Australian J. Exper. Biol. and M. Sc.*, **6**, 301.
HORNBY, H. E., Annual Report of the Department of Veterinary Science and Animal Husbandry, Tanganyika Territory, for 1934, p. 17.
VAN SACEGHEM, R. (1915), *Bull. Soc. path. exot.*, **8**, 351; (1934), *Bull. Agric. Congo Belge*, **25**, 590.

Section of Obstetrics and Gynaecology

President—CLIFFORD WHITE, F.R.C.S.

[April 16, 1937]

The Initiation of Respiration in Asphyxia Neonatorum

A Clinical and Experimental Study Incorporating Fœtal Blood Analyses and a Consideration of Important Methods of Resuscitation.

By ROBERT A. WILSON, M.D., F.A.C.S., M. ALLEN TORREY,
B.S., M.D., and KATHERINE S. JOHNSON, A.B.

(From the Department of Obstetrics and Gynaecology, the Methodist Episcopal
Hospital,¹ Brooklyn, New York)

THE initial gasp after birth is normally a vigorous inspiratory effort that opens the airways and some of the alveoli of the lungs. It is the most important event in every life, and is quite distinct from subsequent respirations. Once breathing, however irregular and shallow, has developed, effective means of augmenting it are available, but there is no one generally accepted measure for initiating the first inspiration. If this does not occur spontaneously, the life of the child depends upon the measures employed.

The onset of respiration is believed to be caused by chemical, rather than by physical factors. An explanation of this phenomenon satisfactory for our purpose is, that immediately after delivery, the placental circulation is markedly impaired by the contracting, retracting uterus. This results in a diminution of the oxygen supply to the baby and a marked increase of the carbon-dioxide tension in the blood which stimulates the respiratory centre to action. We are all born in a condition of apnoea, but it is only when this state persists for an unduly long period of time that there is cause for alarm. In the majority of prolonged apnoeas the constant increase in the carbon-dioxide tension, plus the measures employed by the obstetrician, result in an inspiratory gasp, and apprehension is relieved. More and more often this favourable outcome is not experienced so easily—sometimes, not at all. It is in an effort to face this problem that this paper is presented.

We shall deal only with severe cases of respiratory depression and asphyxia. Clinically most of them correspond to what is known as "asphyxia pallida", which term will be frequently employed. At other times we shall use the word stillborn, indicating in either case a baby in a state of shock, very pale, with a relaxed musculature and absent superficial reflexes, who has not breathed, but whose circulation persists. As far as treatment is concerned there is another class of babies: those which are so deeply narcotized and anaesthetized as to be in serious danger. Although

¹ The investigation was aided by a grant from the Lindredge Research Fund of the Hospital.

these are not in shock and are blue rather than white, such a severe degree of depression presents a problem almost as serious as that of true asphyxia pallida.

Since the literature is replete with studies of the ætiology and pathology of asphyxia neonatorum, these phases will not be dwelt upon. It is important, however, to discuss—briefly—changes in the blood which are found in asphyxia neonatorum. It is only when such studies, at least as far as the oxygen content is concerned, are furnished that a true picture of the gravity of a case can be obtained, and the success or failure of the method of resuscitation properly evaluated. Eastman [9] has shown that in severe degrees of asphyxia neonatorum there is a reduction in the oxygen content of the foetal blood to extremely low levels. He has shown also that the serum pH is markedly reduced, there being at the same time a considerable increase in the carbon-dioxide tension with, usually, a moderate decrease in the carbon-dioxide content. When the latter occurs there is always an increase of endogenous lactic acid, sometimes to very high levels (45 to 90 mgm. per 100 c.c.). Levels above the latter figure are practically always associated with foetal death. For several years previous to the publication of Eastman's studies we conducted similar investigations. Eastman's work was performed on blood from the umbilical artery and vein, as well as on blood from the maternal vein. He reported findings on normal and asphyxiated babies together with those born of deeply anaesthetized mothers. Our studies were on the umbilical vein blood of normal and asphyxiated babies. The first group consisted largely of spontaneous births, while the second was composed of many types of deliveries, avoiding as far as possible, the complicating effects of anaesthesia and narcosis. The blood, obtained under oil by a special technique and analysed by methods similar to those of Eastman, furnished results closely parallel to his. An interesting finding was the low oxygen content in some babies who appeared to be breathing fairly well, while in a fatal case the oxygen content was below one volume per cent.

Pressure from the laity has forced the profession to increase the use of analgesia and anaesthesia. In many hospitals few labours are carried through with no drugs whatever. From a clinical point of view it must be admitted that, although the incorrect or excessive use of drugs may cause anxiety, as a rule such babies respond after a more or less prolonged period of apnoea. Occasionally, however, a depression is encountered which is so deep that after a few shallow respirations the apnoea recurs and such babies can be kept alive only with the greatest difficulty. The important point is, that although few lives are lost as a result of the use of drugs *per se*, such babies cannot stand much additional asphyxia. If in such cases obstruction occurs in the cord, or there is partial separation of the placenta, compression of the head with forceps, &c., plus a long, deep anaesthesia, many of these babies will die. *They would often recover from the narcosis or the asphyxia alone, but are overwhelmed when one is superimposed upon the other.* If a traumatic delivery under deep anaesthesia is anticipated, or if other causes of asphyxia are present, or likely to occur, it would be safer to dispense with drugs.

THE INFLUENCE OF DRUGS ADMINISTERED TO THE MOTHER UPON THE ASPHYXIA OF THE NEWBORN

It is a poor use of drugs which, in sparing the mother pain, causes her to bear a baby that will not breathe. Resuscitation has an important place in the technique of the obstetrician, but it is best that it should be seldom needed. It is not always successful.

All anaesthetics, hypnotics, and narcotics diminish the sensitivity to stimuli, but these drugs vary widely in the relative degrees to which they depress sensitivity to the various kinds of stimuli.

The two most important forms of stimuli in parturition are first, those irritations

of afferent nerves which produce pain, and secondly, those chemical stimuli which act upon respiration. In general the volatile anaesthetics decrease sensitivity to afferent stimuli, while exerting comparatively little influence of a depressant character upon respiration, unless administered in excess. Morphine—the drug traditionally relied upon to relieve pain by diminishing sensitivity to afferent stimuli—exerts a more powerful depressant effect in decreasing the sensitivity of the respiratory centre to stimulation by the gases of the blood.

Obviously for use in parturition the drugs employed should have a maximum capacity to protect against pain, with a minimum tendency to depress respiration. The failure to consider this point is probably due to the fact that until comparatively recent years the drugs chiefly employed were the volatile anaesthetics. Beginning some twenty years ago, however, scopolamine with morphine came into use and the more recent introduction of the barbituric-acid compounds has led to a widespread and increasing practice of prolonged narcotization of the mother, instead of temporary anaesthesia.

Experience demonstrates that most drugs administered to the mother pass also to the child. Consequently the decrease of the sensitivity of the mother is accompanied by a decrease in the sensitivity of the respiratory centre of the child to those chemical stimuli that normally induce and maintain respiration. How important this point is in actual practice is strikingly demonstrated by the figures recently published by Irving [17] and his associates, showing that of all children born of wholly undrugged mothers, less than 2% fail to breathe spontaneously; on the other hand with some of the drugs now frequently used, the depressant effects are so powerful that a large minority, or even a majority (35–65%) of the children born under their influence fail to breathe immediately at birth. Doubtless no obstetrician would admit that the use of such drugs had, in his experience, actually cost the life of a child, but considering the extent of the present use of powerful respiratory depressant drugs in labour, there can be no question that there is a considerable mortality from this cause. This does not take into consideration those babies which are successfully resuscitated, but later develop pneumonia from a continuance of partial atelectasis.

As an approximation, the amount of protection against pain in relation to depression of respiration of drugs and gases in common use is as follows: Paraldehyde, nitrous oxide, ethylene, ether, chloroform, barbiturates, scopolamine-morphine, morphine. When morphine is used, it should be in moderate dosage and should not be administered less than two hours before delivery. We have found, experimentally and by clinical experience, that babies are not easily depressed by the barbiturates, but if deep depression exists as the result of excessive dosage, the response, if any, to the administration of carbon-dioxide is poor. Ether is relatively safe unless present in the blood in high concentration for a long period of time. Nitrous oxide is of little danger to the baby if 15% or more of oxygen is administered with it. If the oxygen ratio is much below this, however, asphyxiation of both mother and baby will occur. The value of paraldehyde is becoming generally recognized. There is no other available drug so harmless.

OLDER METHODS OF RESUSCITATION

Artificial respiration.—Moncrieff [23] says that: "Artificial respiration, in the sense of moving the chest, even gently, stands condemned in any form until respiration has begun, and once a breath has been taken, it is no longer necessary." It does not reflect credit on the profession that this measure is still advocated in most of the standard textbooks. Artificial respiration depends principally for its effectiveness upon compression and a resulting decrease in size of the thoracic cavity. If the alveoli contain air, some of it is expelled, so that when the pressure on the chest is

removed, provided obstruction is not present, the elastic recoil, plus the tonus of the diaphragm, bring about an inspiration of air. It is of no avail to compress the unexpanded, solid, fetal lung, since, upon release of the pressure, air will not enter the dense viscus. In serious cases tonus is almost entirely absent, and if a little air has already entered the bronchial tree, compression further restores atelectasis.

To summarize: Artificial respiration, in the babies under consideration, is condemned for its futility, exposure to cold, and the risk of injury. The peripheral stimuli which are, incidentally, involved in the various methods, are quite useless because they do not reach the centre. The necessary stimuli must be chemical rather than physical.

Mouth-to-mouth insufflation.—This method of resuscitation dates back to antiquity. The principle involved is somewhat similar to that employed in the pulmotor and lungmotor. Mouth-to-mouth insufflation carries serious risk of infection and depends largely for success on the experience and skill of the operator. The latter's mouth serves as a mask, and air is forced into the baby. It usually enters the stomach, but if sharp, short, repeated puffs are made, a little may enter the trachea, especially if the head is held in hyperextension. Some observers believe that the carbon-dioxide in the exhaled air which is between 3.7 and 5.5% may be responsible for a favourable result. This is most unlikely. The oxygen (11–17%) is of some value. This is indicated by improvement in the cardiac impulse sometimes noticed though no respirations occur. When a response is obtained, it is more apt to be due to the fact that a faint reflex is produced by the sudden distension of the larynx and trachea. In severe cases this reflex is not present, so that the principal benefit that might be derived is from bringing into play the Hering-Breuer reflex by a marked distension of the bronchial tree. The pressure of air necessary to affect the stretch receptors, however, is likely to injure the delicate lung tissue.

Summarizing: In the hands of the novice mouth-to-mouth insufflation is always dangerous, and even after long experience, the possibility of ruptured alveoli and infection is great. Occasionally a baby is saved by its use. It should be reserved as a last resort after all other methods have failed.

NEWER METHODS OF RESUSCITATION

In order to evaluate the methods at present available to initiate respiration it is important to describe briefly certain experimental work performed by us. It was carried out in an attempt to answer the following question: Can the alveoli be safely opened and made available for gaseous interchange, by means of gases under pressure in the trachea and bronchial tree (intrinsic pressures)? Conditions closely approximating those found in the living but non-breathing newborn can be obtained by using true stillbirths. Our material consisted of full-term stillbirths in which death occurred less than three hours before delivery. These stillborn infants were immediately intubated with a leak-proof tracheal tube and the bronchial tree was distended by oxygen. Five cases are reported here, a number sufficient to answer the question just propounded. The first infant was intubated for twenty minutes, a continuous pressure of 18 mm. of mercury being used; the other four, with the same pressure applied intermittently—four seconds on and three off. A pressure as high as 18 mm. was used in order to ensure the thorough distension of the bronchial tree. The babies were immediately autopsied and the lungs in all five cases presented no gross evidence of aeration. They immediately sank when placed in water. This is the more remarkable if we bear in mind that during the insufflation the thoracic cage—and, to a lesser degree, the abdomen—were rhythmically expanded and deflated in a manner similar to normal respiration.

When these and other cases in which the pressures ranged from 18 to 5 mm. of mercury are published, the microscopic findings and concomitant photomicrographs

will be given in detail. It is sufficient to state that only relatively few alveoli contained air. When air was found, the surrounding alveolar wall was usually torn, often communicating with other alveoli similarly damaged. Many were filled with blood. In two cases air blisters beneath the pleura were present, indicating extensive damage. The pressure was evidently too great for the friable foetal lung and resulted in serious damage, yet it was not adequate to aerate the lung and open the alveoli. It is logical to assume that a lower pressure, unlikely to damage the tissues, would be less effective in overcoming atelectasis. As a result of our experiments we can positively state that, although the bronchial tree can be thoroughly distended, the chest walls expanded, and the diaphragm displaced, the lung tissue itself cannot be adequately aerated even by pressures high enough to be injurious and destructive.

Drinker respirator.—The efficacy of this respirator for respiratory depression in an adult, or in a child who has breathed, is beyond question. The important point in such cases is that alveoli are open so that, if respiratory movements are even an approximate prototype of the normal, air will enter and leave the alveolar spaces. Exposure is avoided, there is an absence of trauma, and the rhythm is perfect. Although the respiratory movements are not exact duplicates of those controlled by impulses from the centre, the imitation is close.

The diaphragm is an important factor in respiration, but with the Drinker respirator the amplitude of its descent is much less than in normal respiration. In spite of this, numerous reports are favourable and show that good ventilation can be maintained. When this instrument is properly used, in moderately depressed babies, similar favourable results are obtained. We are faced with a more difficult problem in the case of the baby which has never breathed. The collapsed lung of the newborn is a structure composed of the bronchial tree, alveoli, blood-vessels, and fibrous and elastic tissue. It contains no air and does not open suddenly when the chest is expanded but, rather, in sections of varied extent. With each early inspiration additional alveoli are aerated and as this aeration continues, more and more blood from the pulmonary artery circulates in the peri-alveolar capillaries. Gaseous interchange between the alveolar air and the blood now takes place, so that increasing amounts of oxygen are carried to the centre. Roentgenograms show that days, and even weeks, may elapse before the lung is completely expanded.

Coryllos and Birnbaum [5] found that a pressure of 14 cm. of water was necessary to inflate the atelectatic lung of the dog. This pressure was required solely to overcome the cohesion between the opposing surfaces of the collapsed alveoli. We have to take into account the additional pressure needed to overcome the resistance of the chest wall and diaphragm. This introduces an important principle, namely, that the initial effort necessary to expand the lungs must be considerably greater than the subsequent efforts required to maintain the expansion and continue ventilation.

It should be clearly understood that we are only evaluating the use of the Drinker respirator for initiating respiration. Murphy, Wilson, and Bowman [26] in 1931 reported 35 infants treated with this apparatus. In 1932 Murphy and Sessums [25] reported a larger series of 66 infants who failed to breathe promptly at birth. After careful clearing of the air-passages the instrument was adjusted to give a breathing rate of 45 per minute for one group, and 35 per minute for the other. The negative pressure employed was from 8–10 cm. of water. Analysis of the results reported by these workers is not impressive. Fifteen of the 66 infants never breathed and 21 breathed before or during treatment only to die in the hospital. Although at least 13 of the 36 failures were premature, and most of these non-viable, the cause of death in as many as 15 full-term or only slightly premature babies is reported as cerebral hæmorrhage. Tentorial tears were observed in five of the cerebral injury cases, each of which was a breech delivery, but no mention is made of the extent or location of the hæmorrhage in these or the remaining 10, and, as cerebral hæmorrhages are a common finding in asphyxial stillbirths (this condition being shown by Leff [21]

to be a result rather than a cause in most instances), death is not necessarily explained. In accounts of these deaths and others listed as being due to prolonged labour, prolapsed cord, and so on, the important evidence as far as this method of resuscitation is concerned, namely, the extent of lung aeration, is not mentioned.

In 1933 Murphy and Bauer [24] reported the results of post-mortem examinations on the thoracic cavities of infants who died after treatment with a negative pressure of 8-10 cm. of water. They were disappointed to find a high proportion of cases in which large areas of lung were unexpanded. They suggested, as a result of these findings, that better results would probably be obtained if a greater negative pressure were used. In view of these results, and of others equally disappointing received in personal communications, it is evident that the negative pressure should be increased. Serious damage, however, can be inflicted by high degrees of negative pressure, since it is possible to expand the chest to such an extent as to rupture most of the alveoli in the lungs. It has been suggested that better results would be obtained if, in addition to a greater negative pressure, an alternating positive pressure were substituted for the return to atmospheric levels. This is not difficult to accomplish and is undoubtedly an improvement. The objection, even if this is done, that the patency of the air passages is not properly maintained, can be overcome by the simultaneous use of a tracheal tube. The principal difficulty is that, even in conjunction with a tracheal tube and alternating positive pressure, the initiating negative pressure necessary to expand the collapsed lung is greater than has yet been suggested, and cannot be known until extensive experimentation has been performed. Assuming that the expansion is accomplished by an adequate but safe pressure, it would then be important to diminish immediately the expansion force. This would make a trained attendant a necessity. The respirator is cumbersome and expensive, so that even if the technique is eventually perfected, it could hardly be available in many deliveries.

Summary: The Drinker respirator, as employed to-day, has little if any place in the initiation of respiration in the newborn. Piper [29], after years of use and observation with this respirator, came to the following conclusion: "This method of resuscitation based upon the principle of a vacuum can be of no value in those cases either blocked by a mucus plug or in which there is a definite condition of atelectasis. On the other hand, we are convinced that the Drinker apparatus for infants is of great value for the reviving of the newborn infant who has once had normal respiratory action". This is seen in prematures who sometimes have syncopal attacks in the respiratory centre, and in deeply narcotized babies who breathe for a time and then relapse into apnoea.

Lungmotors, pulmotors, resuscitators.—These machines are of two types: (1) Those employing intermittent positive pressure, and (2) those using intermittent positive and negative pressures. It is not within the scope of this paper to consider their value for the adult or for the child who has previously breathed; we are concerned only with the baby that has had no respiratory action and appears unlikely to breathe without definite assistance.

For many years the idea of blowing air or oxygen into the lungs has appealed to science. The earlier pulmotors were given an extensive and fair trial and possibly did save some lives. They have been condemned on at least two occasions, however, by eminent commissions appointed to investigate their claims, and they are little used to-day. The damage inflicted on the living subject, and the number of lives lost because of the delay in instituting other measures, will never be known. Brickley [3] is quoted as having found tears and hæmorrhages in the lungs, following their use in animals. There is no question that many of the resuscitators on the market to-day are superior to the original pulmotors. They are safeguarded against excessive pressures, but the reasons which counsel their abandonment have not changed. On March 14, 1935, an English authority, Moncrieff [23], speaking before the Royal College of Physicians in London, on respiratory failure and resuscitative measures,

stated that: "Positive pressure inhalatory methods involving the use of a mask and pump are unsafe in most instances and quite unsuitable." Most of these machines are clumsy and expensive, and even if they were efficient would not be commonly found in smaller hospitals, and would practically never be on hand in the home, in which the majority of deliveries still occur.

Kreiselman, Kane, and Swope [19] have reported good results with a resuscitator which they designed and developed. By means of a tube running to the back of the mouth and attached to a tight-fitting rubber mask, repeated blasts of oxygen are injected under carefully regulated pressures. Its mode of action appears to be identical with that described under "mouth-to-mouth insufflation", without the disadvantages and dangers of the latter. In order properly to evaluate these authors' work, detailed microscopic studies on the lungs of fresh stillbirths, treated with this machine and then immediately autopsied, should be published. This also applies to any resuscitator which is claimed to open alveoli.

It is not difficult to account for the good results reported by some clinicians in their experience with resuscitators. If the apparatus employs positive and negative pressures, as most of them do, it is generally demonstrated by means of a non-elastic bag made of rubberized fabric. The bag is inflated until it resists further distension and creates a back pressure, which then actuates a reversing mechanism so that an aspirator is brought into play and suction produced. When the bag is empty, the aspirator is automatically shut off, and inflation again instituted. The bag is thus successively inflated and deflated. Inflation and deflation of such a bag is deceptive, because the bag, unlike the air passages of the body, offers little resistance until full. As soon as the inspiratory blast meets an obstacle in the air passages, it is automatically cut off and turned into expiration; thus efficient inspirations are not performed. There follows a rapid clicking of the mechanism back and forth without any visible excursions of the chest and abdomen. Some observers believe that alveoli are gradually opened during this clicking process, but from our experiments on fresh stillbirths, we are convinced that the alveoli cannot be opened in this manner.

When the opportunity to try out a new resuscitator presents itself, some obstetricians are likely to use it on baby after baby, which after delivery present a period of apnoea, regardless of whether such treatment is really necessary (i.e. relaxed musculature, shock, absence of reflexes, failing circulation). As comparatively few babies manifest these findings but, rather, a mild depression as the result of drugs and anaesthesia, it is inevitable that the results will be good. An objection to the use of these machines is that valuable time is lost before such instruments are put aside. *The lapse of even one minute in the case of a severely damaged respiratory centre will result in further damage and may render the cells irreversible.* Schmidt [30] believes this to be due largely to the accumulation of products of incomplete oxidation. Once it has occurred, the full restoration of oxygen will fail to bring back functional activity because the altered cells are no longer able to utilize the gas.

Summary: At times resuscitators appear to give results in cases for which they are not needed. In the serious cases under consideration they usually fail and are always contra-indicated if they employ suction, for if this acts at all, it tends to deflate the lungs and restore them to atelectasis.

Inhalators.—The treatment of asphyxia with an inhalator usually consists of the inhalation of varying percentages of carbon-dioxide and oxygen. Oxygen not only nourishes but also sensitizes the cells of the respiratory centre, while carbon-dioxide, if present in sufficient quantity, stimulates them. Respiratory stimulation may be reflex or chemical. This form of treatment relies on the latter. Without going deeply into the chemical control of respiration, it should be pointed out that, although a slight diminution in the oxygen content of the blood temporarily stimulates the centre, a further diminution renders it less sensitive to whatever carbon-dioxide is present. When this condition persists, oxygen should be restored as rapidly as possible,

but until this has been accomplished an increase in the carbon-dioxide tension will provide increased stimulation and largely compensate for the oxygen lack. If the oxygen content remains relatively low for a long period of time, which is the case in the later months of gestation, a considerable increase in the carbon-dioxide pressure—a normal finding during these months—may not be adequate to initiate or continue respirations, since, as has been shown by Eastman [9], the fetal centre becomes dulled or insensitive to considerably increased tensions of carbon-dioxide. In order to improve the function of the centre the oxygen supply must be fully restored and, for a time, the carbon-dioxide tension, already high, markedly increased. It is, in part, upon these facts that the value of the inhalator for the poorly breathing baby is based. As a rule a mixture of carbon-dioxide and oxygen, containing 10% of the former, is sufficient to augment respiratory movements, but in some few cases in which the respirations are very shallow, in spite of a high carbon-dioxide tension, mixtures containing as much as 20 or even 30% may, for a short time, be employed. As the oxygen revivifies the centre, less carbon-dioxide is needed; thus it should be progressively cut down to 10, or 7, per cent.

As early as 1920 Henderson [14] advocated the use of such mixtures. On numerous occasions since, he and many others have elaborated upon the subject so that, as far as the asphyxiated but breathing baby is concerned, inhalator therapy, when obtainable, has practically supplanted other methods. In such a case we rely on the infant inhaling the gases, thus producing stimulation as well as oxygenation of the centre. The inhalator has saved, and will continue to save, countless babies, yet it can actually do harm. This statement is based upon the fact that the inhalator is useless in a stillborn child for, placing a mask over a baby's face, even when the gas is under pressure, will not assure its entering the lungs. Valuable time is thus lost if the limitations of the inhalator are not appreciated.

To summarize: The inhalator is the best and safest means we have for saving the life of the asphyxiated but breathing baby, and is also of value as a neonatal treatment for the prevention of atelectasis and pneumonia. It is, however, of no avail in itself as a means of initiating respiration (Table I, pp. 78 *et seq.*).

Laryngeal intubation and insufflation.—The digital insertion of a flexible rubber tube into the trachea has been practised for many years, ease of introduction depending principally on the presence or absence of a laryngeal reflex. If present, it indicates a comparatively mild asphyxia, so that although insertion might be difficult, it is rarely needed. When the reflex is absent, there are no respiratory efforts and the skeletal muscles are markedly atonic. Because of this such babies can be intubated with little practice—De Lee [7], for example, mentions a simple technique. In 1928 Flagg [13] described a technique for introducing a metal tube into the trachea by means of a small electrically lighted laryngoscope. The tracheal tube is connected to a water manometer which is in turn connected with a supply of carbon-dioxide and oxygen. The manometer indicates the pressure of the gases in the tube and is so adjusted as to act as a blow-off valve if an excessive pressure is used. We have found that 12 mm. of mercury is the highest pressure that can be used with safety. Blaikley and Gibberd [2] have recently suggested a somewhat similar technique employing a rubber catheter instead of the rigid tube. Although trauma may be inflicted if the laryngeal reflex is present, in its absence both methods are easy and safe.

The lungs of the stillborn are dark in colour, do not crepitate, and sink in water. With the first inspiration the thoracic wall expands and the diaphragm descends so that a disproportion is created between the thoracic cavity and the solid lungs. In the absence of obstruction, air enters the bronchial tree and infiltrates into the alveoli. There is little or no negative pressure in the pleural space at this time, since insufficient disproportion between the lungs and the chest cavity exists. Later, as a result of the rapid growth of the ribs and vertebral column, a real disproportion is

present which, because of the elastic recoil of the lung tissue, produces a definite intrapleural negative pressure.

To most obstetricians intratracheal insufflation has for its principal object the forcible expansion of the lungs. It has been previously stated that the alveoli cannot be safely opened in this manner. The preceding paragraph described Nature's way of opening the lungs, which, in most respects, is at variance with the concept of using gases under pressure in the trachea.

This does not mean that insufflation is not of great value. On several occasions we have observed that when oxygen is insufflated into the trachea there is a definite improvement in colour. If the insufflation is performed with a tight-fitting tube and a pressure as low as 5 mm. of mercury, the bronchial tree is distended, the chest increased in size, and the absorption of oxygen even more rapid. Using this pressure and technique we kept a baby alive for two hours although it never breathed, and autopsy revealed no open alveoli. This is of great significance. Intermittent pressure is recommended by Flagg, but Blaikley and Gibberd state that this is not necessary. They feel that if respiration commences, expiratory movements against a positive pressure assist in the aeration of alveoli and to some extent are imitations of the valuable crying efforts. Intermittent pressure is probably of value, however, as the rhythmic expansion of the bronchial tree may bring into play the Hering-Breuer reflex. Although this reflex is absent in severe cases, it will return if the circulation improves sufficiently *as a result of the absorption of oxygen by the mucosa lining the trachea and bronchioles.*

To summarize: Intubation is safe and easy to accomplish in the severely asphyxiated baby, permitting thorough aspiration and providing an excellent airway. Essentially, it is the extension of an inhalator into the lungs. It should not be used in an attempt to open the alveoli by direct attack.

Tilting boards.—Eve [12] and Cornish [4] have devised see-saws on which the patient is laid and rocked through an angle of thirty or more degrees. Henderson [15] in recent experiments on dogs, found that the volume of air moved in and out of the lungs by this rocking method is much less than that displaced when the chest is compressed by hand. As such pressure is useless when there is no air to expel, it would seem that the rocking method is of little or no value in initiating respiration.

Intravenous resuscitation.—By this is meant the initiation, or re-initiation, of respiration, utilizing a substance injected into the blood-stream. This method depends principally either upon direct stimulation of the respiratory centre or upon the lowering of the response threshold, so that a previously dulled centre is rendered more sensitive to the prevailing carbon-dioxide in the blood. In 1928 one of us (R. A. W.) [39] presented a preliminary report on the injection of a respiratory stimulant into the umbilical vein for the treatment of asphyxia neonatorum.

In the search for a satisfactory agent much time was devoted to the study of drugs commonly deemed to be analeptics and respiratory stimulants, such as strychnine, epinephrin, caffeine sodio-benzoate, atropine, ephedrine, &c. Either there was no respiratory stimulation following injection, or it was so slight that these drugs would be of little use in a severely asphyxiated baby. Undesirable and dangerous side actions were often found, particularly with the dosage increased in order to obtain more respiratory effects.

It is necessary to summarize the results of hundreds of animal experiments in different types and degrees of narcosis and asphyxia in a short space. Only two drugs were found to be good respiratory stimulants: Pyridine-B-carbonic acid diethylamide (coramine) and lobeline hydrochloride. The former increased considerably the rate and amplitude of respiratory movements. On a number of occasions it initiated respiration after the experimental production of apnoea. Frequently, however, severe and sometimes fatal convulsions occurred even when recommended dosage was used. Moncrieff [23] speaks of similar convulsions in children, thus we

have not felt justified in using it intravenously in the newborn. These convulsions do not usually occur in adults and older children, when the drug is injected subcutaneously. No further consideration was given to coramine, as the subcutaneous injection of this or any other drug in stillborn babies is doomed to frequent failure because of the weak circulation and the consequent lapse of time which results between injection and effect. If a favourable result is to be obtained within a few seconds after injection, it is possible only by intravenous therapy. (Pentamethylentetrazol (metrazol) and picrotoxin are known to be respiratory stimulants. In the case of the newborn extreme caution is advisable, for these drugs are classed as convulsants.)

There is general agreement among those who have had experience with lobeline that it stimulates respiration. There is some difference of opinion as to its effectiveness in severe degrees of narcosis and asphyxia. Competent observers [1, 6, 8, 10, 16, 32, 33, 35, 36, 37, 38, 39, 40] have reported more or less favourably, yet others [11, 18, 20, 22, 27, 28, 31, 34] have advised against its use. We have given it a thorough and impartial trial both clinically and in the laboratory, using a preparation of lobeline hydrochloride.¹ The results as a whole have been impressive, especially in severe asphyxias.

Graphs of the apnoea and early respirations of the newborn have not been previously produced, yet they are absolutely necessary if we wish to have impartial and permanent evidence of the condition of a baby before and after resuscitation. As there was no reliable method for recording the respiration of the newborn immediately after birth, it was necessary to devise an apparatus for that purpose. It consists of a receptacle in which the infant is placed immediately after delivery. Movements of the infant's chest and abdomen are transmitted to a spirometer carrying a scribing point which in turn writes on a drum (fig. 1). By means of this apparatus it is possible to study, not only the effects of drugs and gases as resuscitant agents, but also the effect on the baby of drugs and anaesthetics administered to the mother before delivery. Tracings can be started as soon as seven seconds after delivery.

We have proved by means of the aforementioned graphs that lobeline will heighten the respiratory efficiency of the normally breathing baby; that it will rapidly overcome respiratory depression due to morphine; that it will produce such a marked expansion of the thoracic cavity as to greatly diminish, if not entirely overcome, residual atelectasis; lastly, that it will actually initiate respirations in serious asphyxias. The graphs of the latter condition are fortified by detailed protocols of the resuscitation of ten cases of asphyxia pallida with concomitant fetal blood studies (Table I, pp. 78 *et seq.*). The best technique of injection, blood-pressure response, method of action, dosage, and safety will be considered.

In order to duplicate these results the drug must be introduced directly into the blood-stream, a most rapid method for reaching the centre. Even in the breathing child, carbon-dioxide administered with an inhalator finally reaches the centre in this way. (Its entrance into the lungs and passage through the alveolar walls is an intermediate step.) It is, therefore, logical to introduce the stimulating substance directly into the blood if, as it has been previously shown, the lungs are solid. In grave asphyxias the lingual death zone is a barrier to the passage of gases into the trachea. The desired effect need only be of short duration because, if respiration commences, and the airways are patent, a few inspirations will open up alveoli to oxygen and carbon-dioxide. Treatment is then continued as it would be on any asphyxiated but breathing baby.

Any method of resuscitation should be as simple as possible. This is particularly true in obstetrics, because so many deliveries take place in the home. One should also keep in mind the confusion and excitement that often attends the birth of a stillborn child. The superficial veins are too small to be readily available, and

¹ For a detailed history and description of this drug, the reader is referred to the standard textbooks of pharmacology.

injections into the longitudinal sinus or heart chamber are radical procedures and should not be lightly undertaken. The umbilical vein offers the most convenient place of injection. Only when the cord has been cut close to the child need other sites be considered. We make it a practice always to leave the cord long until respirations are well established.

The following improved technique is the one recommended for general use.

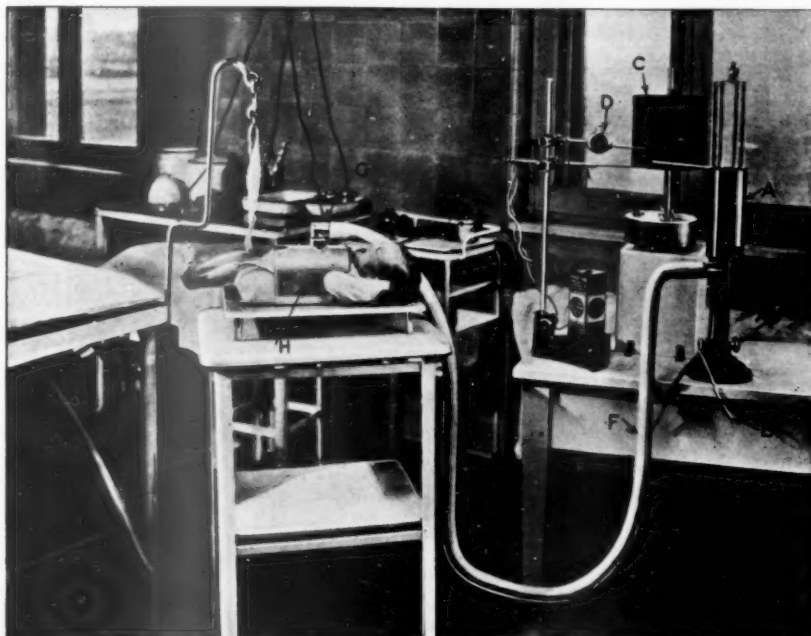


FIG. 1.—Pneumograph connected to recording apparatus. (Baby 3 days old.) (A) Spirometer with scribing point in contact with revolving drum. (B) Clamp in place on small rubber tube through which air is forced into the system. (C) Recording drum. (D) Timer for recording seconds. (E) Electric timer. (F) Rubber tube. (G) Connexion to which rubber bag is attached. (H) Hinged plate under which is inflatable rubber bag contacting front and sides of chest and abdomen.

Note.—When taking tracings immediately after delivery, the pneumograph should be nearer the delivery table, so that the cord need not be cut unless it is very short.

Although not difficult, it must be correctly understood and performed in order to obtain a speedy and satisfactory response :—

Immediately after delivery the baby is handed to an assistant who holds it, preferably, by the feet with the head down. The cord should not be cut unless it interferes with delivery or is very short. As previously mentioned, it should not be cut close to the umbilicus. Thorough aspiration with a flexible rubber tube is performed, after which a careful appraisal of the baby is made. Particular attention should be paid to the colour, muscle tonus, and strength and rate of the cardiac impulse. If resuscitation is decided upon, the cord is inspected and a good injection site determined upon. This should be prefer-

ably between 6 and 8 in. from the umbilicus. The cord is then doubly clamped about $1\frac{1}{2}$ in. distal to the chosen injection site and cut between the clamps. The remainder of the technique may be carried out on a table or in a heated receptacle, but we prefer to perform it without moving the baby, keeping it in its inverted position. There is less delay and less danger of a break in asepsis. An exception to this is made in the case of grave asphyxias where a more elaborate technique in conjunction with a tracheal tube is used. This will be described later. If lobeline is the resuscitating agent to be used, gr. $\frac{1}{30}$ of the hydrochloride is injected into the umbilical vein (fig. 2) and the cord compressed firmly between

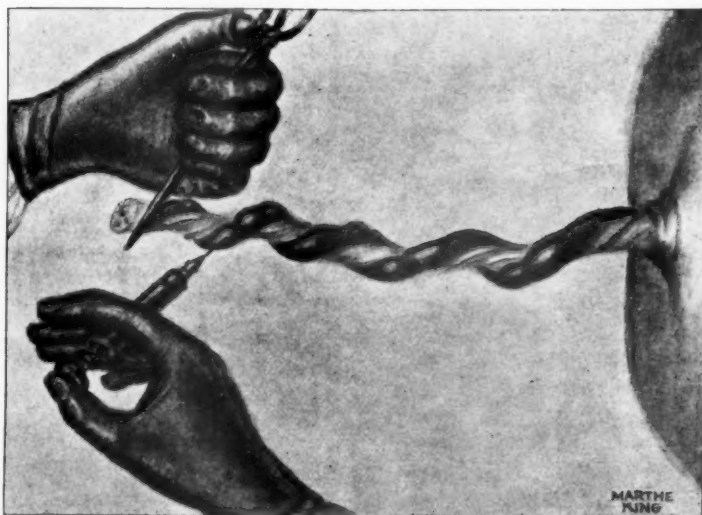


FIG. 2.—Manner of injecting a respiratory or cardiac stimulant into the umbilical vein. The cord has been clamped and cut about 8 in. from the umbilicus. In order to facilitate the insertion of the needle, if possible, a dilated or bulbous portion of the vein should be selected. It is well to withdraw a little blood in order to be sure that the needle tip is within the lumen.

the first and second fingers adjacent to the clamp. The column of blood and drug in the vein is milked towards the umbilicus (fig. 3). (Epinephrin and other drugs may be similarly administered.) The first half of the stripping is done rapidly to avoid delay (the drug has not yet reached the child). The milking is then continued slowly and progressively until a respiratory response results. Once breathing is well established, any drug remaining in the vein is removed by tying and cutting the cord near the umbilicus. According to the preference of the operator, an inhalator mask may be applied before the stripping or after respirations have been induced. Injection into the cord substance or the umbilical arteries is of no avail. In rare cases injection may be difficult if the vein is small or collapsed. The latter condition is easily corrected by having the assistant compress the cord between the fingers at the umbilicus and slide them a short distance toward the clamp. This causes the vein to stand out clearly.

Identification of the umbilical vein.—(1) The umbilical vein is more superficial and larger than either individual artery. (2) The umbilical vein nearly always

discloses points of dilatation and varicosity, and this, in conjunction with its greater size, will identify it. Inject at an area of dilatation.

Blood-pressure tracings from the external carotid artery of the cat show a rather sharp rise, followed by a slow fall, sometimes to a little below the base line with a gradual return to normal. The blood-pressure effects are not significant. Clinically there has been no evidence of either cardiac stimulation or depression. The question is of little importance because as soon as a few respirations have occurred, the oxygenation of the blood brings about an immediate improvement in the circulation.

Lack of space prevents the inclusion of many graphs obtained under widely varying conditions. Some illustrate the effect of lobeline, administered for purposes of demonstration, on normal breathing babies. In one of them, the change in the rate

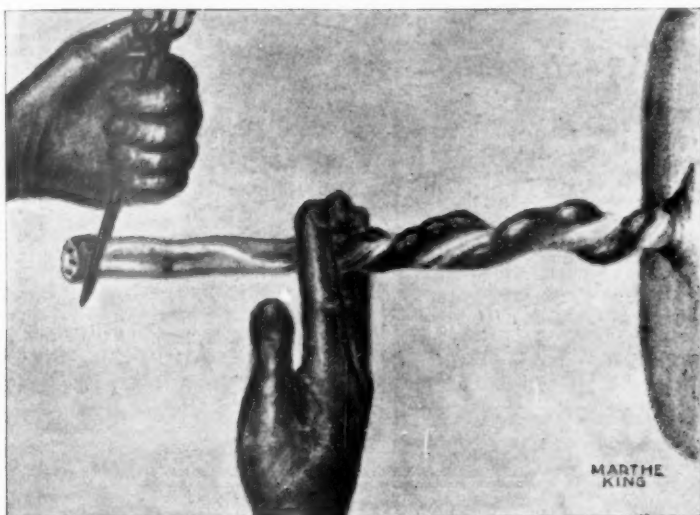


FIG. 3.—Stripping of the umbilical cord. It is compressed between the fingers, distal to the point of injection and the fingers then moved towards the umbilicus. The amount and rate of introduction of a drug into the general circulation are regulated according to the speed at which the fingers are moved.

and amplitude following injection represented an increase in respiratory efficiency of 310 per cent. Excellent results were obtained on infants depressed by morphine and the barbiturates (fig. 4). A glance at such tracings shows a tremendous increase in the amplitude—and, to a less extent, the rate—of the respirations, resulting in the opening of numerous alveoli. The flow of tidal air and gaseous interchange with the blood are therefore proportionately increased. The majority of the graphs illustrate a considerable expansion of the thorax, which is well maintained, a change of respiratory style having been brought about. Breathing now takes place with the chest in an inspiratory position. Atelectasis has been, at least partially, overcome.

This type of graph is useful chiefly to furnish pharmacological evidence. Graphs which illustrate the initiation of respiration are in a different category. Some of them, in conjunction with the clinical picture and blood findings, indicate recovery from apnoeas of a serious nature (fig. 5).

have not felt justified in using it intravenously in the newborn. These convulsions do not usually occur in adults and older children, when the drug is injected subcutaneously. No further consideration was given to coramine, as the subcutaneous injection of this or any other drug in stillborn babies is doomed to frequent failure because of the weak circulation and the consequent lapse of time which results between injection and effect. If a favourable result is to be obtained within a few seconds after injection, it is possible only by intravenous therapy. (Pentamethylenetetrazol (metrazol) and picrotoxin are known to be respiratory stimulants. In the case of the newborn extreme caution is advisable, for these drugs are classed as convulsants.)

There is general agreement among those who have had experience with lobeline that it stimulates respiration. There is some difference of opinion as to its effectiveness in severe degrees of narcosis and asphyxia. Competent observers [1, 6, 8, 10, 16, 32, 33, 35, 36, 37, 38, 39, 40] have reported more or less favourably, yet others [11, 18, 20, 22, 27, 28, 31, 34] have advised against its use. We have given it a thorough and impartial trial both clinically and in the laboratory, using a preparation of lobeline hydrochloride.¹ The results as a whole have been impressive, especially in severe asphyxias.

Graphs of the apnoea and early respirations of the newborn have not been previously produced, yet they are absolutely necessary if we wish to have impartial and permanent evidence of the condition of a baby before and after resuscitation. As there was no reliable method for recording the respiration of the newborn immediately after birth, it was necessary to devise an apparatus for that purpose. It consists of a receptacle in which the infant is placed immediately after delivery. Movements of the infant's chest and abdomen are transmitted to a spirometer carrying a scribing point which in turn writes on a drum (fig. 1). By means of this apparatus it is possible to study, not only the effects of drugs and gases as resuscitant agents, but also the effect on the baby of drugs and anaesthetics administered to the mother before delivery. Tracings can be started as soon as seven seconds after delivery.

We have proved by means of the aforementioned graphs that lobeline will heighten the respiratory efficiency of the normally breathing baby; that it will rapidly overcome respiratory depression due to morphine; that it will produce such a marked expansion of the thoracic cavity as to greatly diminish, if not entirely overcome, residual atelectasis; lastly, that it will actually initiate respirations in serious asphyxias. The graphs of the latter condition are fortified by detailed protocols of the resuscitation of ten cases of asphyxia pallida with concomitant fetal blood studies (Table I, pp. 78 *et seq.*). The best technique of injection, blood-pressure response, method of action, dosage, and safety will be considered.

In order to duplicate these results the drug must be introduced directly into the blood-stream, a most rapid method for reaching the centre. Even in the breathing child, carbon-dioxide administered with an inhalator finally reaches the centre in this way. (Its entrance into the lungs and passage through the alveolar walls is an intermediate step.) It is, therefore, logical to introduce the stimulating substance directly into the blood if, as it has been previously shown, the lungs are solid. In grave asphyxias the lingual death zone is a barrier to the passage of gases into the trachea. The desired effect need only be of short duration because, if respiration commences, and the airways are patent, a few inspirations will open up alveoli to oxygen and carbon-dioxide. Treatment is then continued as it would be on any asphyxiated but breathing baby.

Any method of resuscitation should be as simple as possible. This is particularly true in obstetrics, because so many deliveries take place in the home. One should also keep in mind the confusion and excitement that often attends the birth of a stillborn child. The superficial veins are too small to be readily available, and

¹ For a detailed history and description of this drug, the reader is referred to the standard textbooks of pharmacology.

injections into the longitudinal sinus or heart chamber are radical procedures and should not be lightly undertaken. The umbilical vein offers the most convenient place of injection. Only when the cord has been cut close to the child need other sites be considered. We make it a practice always to leave the cord long until respirations are well established.

The following improved technique is the one recommended for general use.

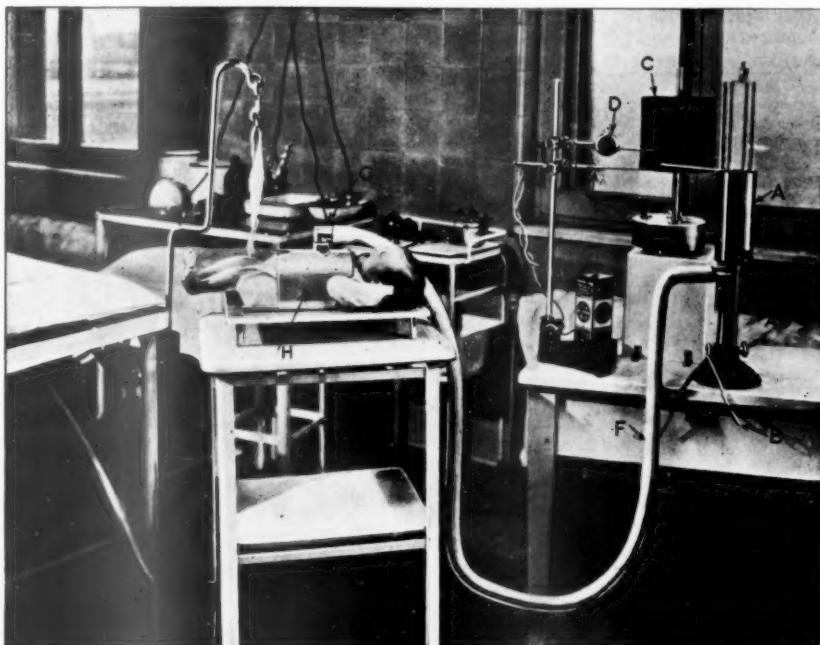


FIG. 1.—Pneumograph connected to recording apparatus. (Baby 3 days old.) (A) Spirometer with scribing point in contact with revolving drum. (B) Clamp in place on small rubber tube through which air is forced into the system. (C) Recording drum. (D) Timer for recording seconds. (E) Electric timer. (F) Rubber tube. (G) Connexion to which rubber bag is attached. (H) Hinged plate under which is inflatable rubber bag contacting front and sides of chest and abdomen.

Note.—When taking tracings immediately after delivery, the pneumograph should be nearer the delivery table, so that the cord need not be cut unless it is very short.

Although not difficult, it must be correctly understood and performed in order to obtain a speedy and satisfactory response :—

Immediately after delivery the baby is handed to an assistant who holds it, preferably, by the feet with the head down. The cord should not be cut unless it interferes with delivery or is very short. As previously mentioned, it should not be cut close to the umbilicus. Thorough aspiration with a flexible rubber tube is performed, after which a careful appraisal of the baby is made. Particular attention should be paid to the colour, muscle tonus, and strength and rate of the cardiac impulse. If resuscitation is decided upon, the cord is inspected and a good injection site determined upon. This should be prefer-

ably between 6 and 8 in. from the umbilicus. The cord is then doubly clamped about $1\frac{1}{2}$ in. distal to the chosen injection site and cut between the clamps. The remainder of the technique may be carried out on a table or in a heated receptacle, but we prefer to perform it without moving the baby, keeping it in its inverted position. There is less delay and less danger of a break in asepsis. An exception to this is made in the case of grave asphyxias where a more elaborate technique in conjunction with a tracheal tube is used. This will be described later. If lobeline is the resuscitating agent to be used, gr. $\frac{1}{30}$ of the hydrochloride is injected into the umbilical vein (fig. 2) and the cord compressed firmly between

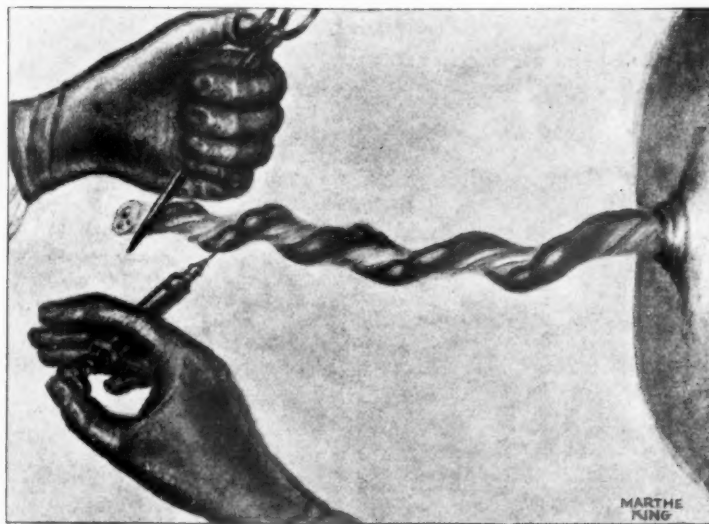


FIG. 2.—Manner of injecting a respiratory or cardiac stimulant into the umbilical vein. The cord has been clamped and cut about 8 in. from the umbilicus. In order to facilitate the insertion of the needle, if possible, a dilated or bulbous portion of the vein should be selected. It is well to withdraw a little blood in order to be sure that the needle tip is within the lumen.

the first and second fingers adjacent to the clamp. The column of blood and drug in the vein is milked towards the umbilicus (fig. 3). (Epinephrin and other drugs may be similarly administered.) The first half of the stripping is done rapidly to avoid delay (the drug has not yet reached the child). The milking is then continued slowly and progressively until a respiratory response results. Once breathing is well established, any drug remaining in the vein is removed by tying and cutting the cord near the umbilicus. According to the preference of the operator, an inhalator mask may be applied before the stripping or after respirations have been induced. Injection into the cord substance or the umbilical arteries is of no avail. In rare cases injection may be difficult if the vein is small or collapsed. The latter condition is easily corrected by having the assistant compress the cord between the fingers at the umbilicus and slide them a short distance toward the clamp. This causes the vein to stand out clearly.

Identification of the umbilical vein.—(1) The umbilical vein is more superficial and larger than either individual artery. (2) The umbilical vein nearly always

discloses points of dilatation and varicosity, and this, in conjunction with its greater size, will identify it. Inject at an area of dilatation.

Blood-pressure tracings from the external carotid artery of the cat show a rather sharp rise, followed by a slow fall, sometimes to a little below the base line with a gradual return to normal. The blood-pressure effects are not significant. Clinically there has been no evidence of either cardiac stimulation or depression. The question is of little importance because as soon as a few respirations have occurred, the oxygenation of the blood brings about an immediate improvement in the circulation.

Lack of space prevents the inclusion of many graphs obtained under widely varying conditions. Some illustrate the effect of lobeline, administered for purposes of demonstration, on normal breathing babies. In one of them, the change in the rate

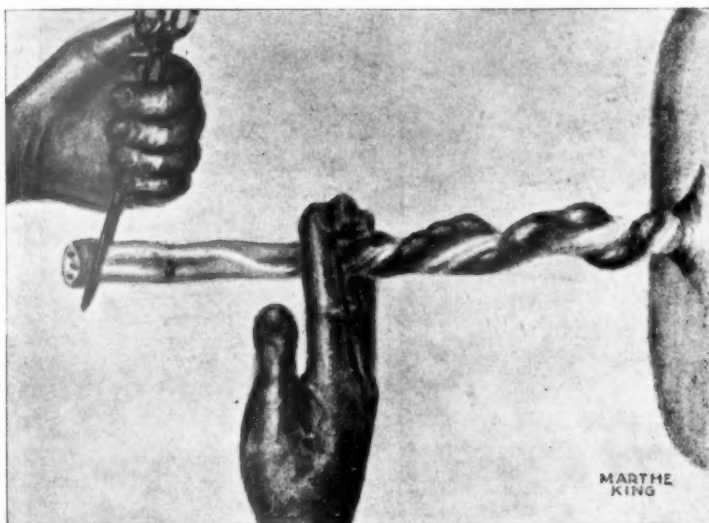


FIG. 3.—Stripping of the umbilical cord. It is compressed between the fingers, distal to the point of injection and the fingers then moved towards the umbilicus. The amount and rate of introduction of a drug into the general circulation are regulated according to the speed at which the fingers are moved.

and amplitude following injection represented an increase in respiratory efficiency of 310 per cent. Excellent results were obtained on infants depressed by morphine and the barbiturates (fig. 4). A glance at such tracings shows a tremendous increase in the amplitude—and, to a less extent, the rate—of the respirations, resulting in the opening of numerous alveoli. The flow of tidal air and gaseous interchange with the blood are therefore proportionately increased. The majority of the graphs illustrate a considerable expansion of the thorax, which is well maintained, a change of respiratory style having been brought about. Breathing now takes place with the chest in an inspiratory position. Atelectasis has been, at least partially, overcome.

This type of graph is useful chiefly to furnish pharmacological evidence. Graphs which illustrate the initiation of respiration are in a different category. Some of them, in conjunction with the clinical picture and blood findings, indicate recovery from apnoeas of a serious nature (fig. 5).

In our experience the best results are obtained after the use of morphine, chloral hydrate, and the barbiturates. In moribund babies, only irregular gasps may follow injection, but these are sometimes adequate to save life. In serious but less profound asphyxias, vigorous and fairly regular respirations are initiated. The effects of the drug disappear in from two to four minutes.

Lobeline acts by lowering the threshold of the centre to the carbon-dioxide present in the blood. The first inspiration takes place within fifteen seconds after milking the cord, if the centre is not irreparably damaged. It is imperative that the drug be correctly administered. Before the respiratory response, there is a stiffening of the entire body frequently resulting in a mild opisthotonus. The inspiratory gasp follows almost immediately. These findings are so constant that if they are absent,

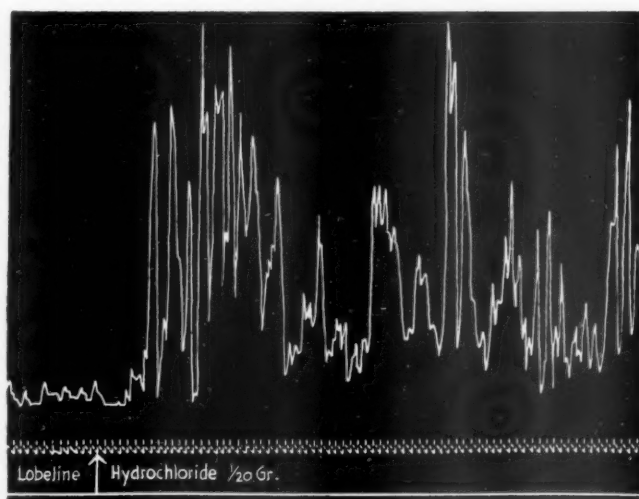


FIG. 4.—Response of a morphinized baby, unexpectedly born 50 minutes after morphine sulphate gr. $\frac{1}{4}$ had been administered to the mother. Spontaneous delivery. No anaesthetic. Baby blue but manifested good tonus. Cardiac impulse slow, regular and strong. Graph started 3 minutes after delivery. Note slow and shallow respirations with a tendency of expiration to lag. Expiratory lagging is a form of respiratory depression often encountered in drugged babies. There are short periods of expiratory apnoea. Such infants unless treated vigorously suffer from atelectasis and are subject to neonatal pneumonia.

it is almost conclusive evidence that the drug is not in the general circulation. The increase of tonus is itself of great value. Certain writers have opposed the use of drugs because of the danger of over-dosage. This is not a valid objection because, if it were, it would be necessary in many diseases, to discard remedies which are poisonous in excess. Over-dosage with the hydrochloride does not result in depression, but only in a temporary apnoea. This is due to a fixation of the chest and diaphragm in the inspiratory position as a result of excessive stimuli from the centre (Wilson and Torrey [40]). This apnoea is in itself harmless, except that the desired pulmonary ventilation does not occur. Since delay in pulmonary ventilation is injurious, the apnoea, for this reason, is undesirable. It will not occur if the dosage is correct. Gr. $\frac{1}{20}$ gives the most satisfactory results, although gr. $\frac{1}{40}$ elicits an excellent response in mild cases. As high as gr. $\frac{8}{20}$ may be employed, although with the

larger amounts the aforementioned apnoea may be encountered. In order to allay apprehension regarding over-dosage, we may state that after careful tests on animals we have used in babies as much as six times the recommended dose without permanent ill-effects.

In this institution up to January 1, 1937, lobeline hydrochloride has been injected into the circulation of 340 babies. A detailed analysis of these cases will be published

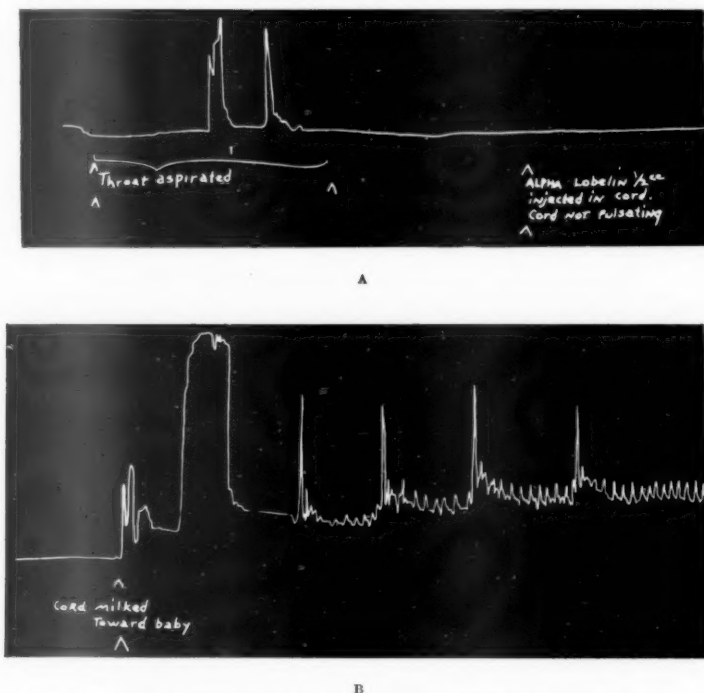


FIG. 5.—A. F., No. 12,535. Weight 6 lb. 13 oz. Gestation 9 months. Labour 16 hours, 7 minutes. Morphine sulphate gr. $\frac{1}{2}$, 2 hours before delivery. Gas-oxygen ether anaesthesia. Spontaneous delivery. Tight knot in cord. Baby pale and flaccid. No pulsation of cord. Slow and faint cardiac impulse discernible. Condition judged critical. One and three quarter minutes after delivery lobeline hydrochloride gr. $\frac{1}{8}$ injected. Cord stripped 52 seconds later. This copy of an original graph shows a prolonged apnoea. The two movements of the scribing point before injection should be disregarded. They were caused by pressure on the bag during aspiration. The apnoea continued until milking, which resulted in a deep inspiration, maintained for 6 seconds. Then a series of inspirations at intervals of about 17 seconds, interspersed with shallow respirations followed. The latter tended to increase in depth and rate. CO_2 7%, O_2 93% administered after removal of infant from pneumograph. Recovery. Oxygen content 1.3 volumes per cent. pH 7.06.

in the future. It should be stated that about 100 of the injections were administered to normal babies in order to secure additional data. All treated babies were subsequently observed by competent pediatricians. In no instance did side effects such as vomiting or convulsions ensue, and no infections of the umbilicus were noted.

Summary: Intravenous resuscitation appears to have only a limited field in the poorly breathing baby, but is of great importance in the stillborn. Its role is almost exclusively that of initiation.

Two highly desirable aims, namely an increase of body tonus and a favourable influence on the respiratory centre, have been satisfactorily achieved by lobeline hydrochloride, which has been found to be safe and free from side effects. Its use in combination with other drugs is, at present, under investigation.

Important advantages of this method are economy, simplicity, and rapidity of action. Disadvantages are the transient nature of the response and the necessity for perfect asepsis.

Discussion

The most important methods of resuscitation have been presented. It is apparent that no one of them is entirely satisfactory. We have found that in combination, however, most encouraging results may be obtained, and suggest *the intravenous use of a respiratory stimulant in conjunction with tracheal insufflation and the subsequent application of an inhalator*. The technique, important particularly in asphyxia pallida, is as follows:—

Immediately after delivery as much material as possible is aspirated with a rubber catheter. The umbilical vein is then injected and stripped to just short of the halfway mark (figs. 2 and 3). A second clamp is, however, applied here to prevent the blood from returning toward the site of injection. So far the initiating substance has not entered the circulation, but has been made ready for subsequent use. The next step consists of introducing a laryngoscope, the baby lying on a table with the head over the edge in hyperextension. Suction of the larynx and trachea is performed, using a hollow sound designed for this purpose, and the tracheal tube then inserted. The latter insufflates a mixture of carbon-dioxide and oxygen in the proportion of 20–80% respectively, under intermittent pressure (5–12 mm. of mercury). If preferred, lesser percentages of carbon-dioxide or pure oxygen may be used. The initiating drug is slowly “milked” into the circulation by further stripping of the cord, a sufficient amount being introduced to bring about a definite gasp and subsequent respirations. The carbon-dioxide entering the newly opened alveoli results in an increase in depth and frequency of the respirations. The oxygen quickly improves the circulation and also renders the respiratory centre more sensitive. When high percentages of carbon-dioxide are used, the tube should be withdrawn in from one to two minutes after breathing has commenced (Cases 9 and 10, Table I), the tongue pulled forward by a clamp or suture, and an inhalator placed over the face. If the lower percentages or pure oxygen are favoured, the tube may be left in place much longer. The inhalator supplies percentages of about 7 and 93 respectively. This treatment is continued until the child is out of immediate danger. In severe cases it is advisable to administer these gases at intervals for approximately five days.

In two cases which came under the care of one of us (R.A.W.) the babies showed no signs of life. Epinephrin was injected directly into the heart. As a result, some faint cardiac pulsations were observed; the preceding technique initiated respirations, and both babies recovered. A number of cases have been reported in which life was saved by the intracardiac injection of epinephrin. If death is not absolutely certain, it should always be tried.

This combined technique embodies advantages of important methods with few of their disadvantages. The tracheal tube overcomes obstruction and, if gases are employed, brings them into the lungs under a safe pressure, ready to be absorbed at the first opening of alveoli. No attempt is made to forcibly dilate the alveoli within. The use of an inhalator, when respirations have been established, is an accepted procedure. It is not imperative to employ varying percentages of carbon-dioxide,

although some writers have claimed important benefits from the brief use of a high concentration. This has been challenged (Eastman [9]). A strength of from 5 to 7 per cent. is effective and, when used, does not require the early removal of the tracheal tube. The technique is effective in any case sufficiently serious to have a diminished or absent laryngeal reflex.

The importance of thorough suction cannot be overestimated. The initial inspiration may otherwise result in inundating the bronchial tree with liquor amnii, blood, meconium, &c., and the baby may drown or die of shock.

From January 1, 1927, to January 1, 1937, during which time the greater part of this study was conducted, 17,860 live babies, from 7 to 9 months of gestation, were born in the Methodist Episcopal Hospital (Table II, p. 81). Among them were many instances of respiratory depression and asphyxia, ranging from mild morphinization to asphyxia pallida.

The 10 cases in Table I are examples of the latter class. In none were drugs administered to the mother less than five hours before delivery. In Case 4 no anaesthetic was used. In the others gas-oxygen with and without the addition of ether was employed. It is our custom to use a minimum amount of ether, therefore the anaesthetic played a minor part as an aetiological factor. Unless otherwise specified the "Simple Measures of Resuscitation" included suction, holding the baby head downward with the head extended, gentle flagellation, and, sometimes, pressure on the chest.

Delay in the employment of more modern methods in a few of the cases is explained by reluctance to utilize unfamiliar procedures. In Case 10 the armamentarium was not immediately available.

It is difficult, of course, to describe satisfactorily the relative severity of each case. Pallor, shock, and degree of tonus vary, and can best be appreciated by those present. With the exception of Case 6 the cardiac pulsation is described. This is a useful index of the extent and duration of oxygen deprivation. The most accurate index of the gravity of a particular case is supplied by a blood analysis which was taken in all but Case 2. Other factors, such as trauma, cerebral oedema, and hæmorrhage, cannot be estimated at the time of delivery. The oxygen content is normally about 12 volumes per cent., and it is remarkable that Cases 3, 7, and 10 recovered. It is reasonable to assume that the low content persisted for only a short time, insufficient to permanently damage the delicate nerve-cells of the centre. On the other hand, in Cases 7 and 10, the content must have sunk lower, for considerable time elapsed between taking the blood and the first inspiration. Considering 7.40 to be a normal pH, some of the readings fell to very low levels hardly compatible with recovery.

The blood was obtained under oil immediately after delivery, before any resuscitative action was taken. The cord was doubly clamped and cut about 8 in. from the baby, and the blood then removed from the placental section of the umbilical vein. In Cases 7 and 10 the cord was clamped and cut before delivery. Oxygen content was determined according to the method of Van Slyke and Neill. The serum pH was measured electrometrically. In many cases, including several in Table I, the total carbon-dioxide content of the blood was determined as well as an estimation of the carbon-dioxide tension. These figures are not given, as we believe the oxygen content to be the factor of prime importance. We wish to avoid any discussion of the relative merits of pure oxygen and carbon-dioxide-oxygen mixtures in primary resuscitation. Cases 1 and 5 were cinematographed, and the film, which includes the resuscitation of other cases, is available for those who are interested.

The question has been raised whether or not intravenous resuscitation should be practised alone, if gas therapy, or at least a tracheal tube, is not available. This is optional when the prognosis appears favourable, even though the depression is deep and the respirations for the time being inadequate. Inasmuch as the graphs show that respiratory efficiency can be increased, and the thoracic cavity expanded by this

TABLE I.—SUMMARY OF THE IMPORTANT FACTS CONCERNING THE RESUSCITATION

Infant	Cause of asphyxia	Delivery	Cardiac impulse	Oxygen content (volumes per cent.)	pH	Simple measures of resuscitation (minutes)	Dose of lobeline (grains)	Elapsed time from tripping to first inspiratory seconds
1 Term	Breech delivery. 14 minutes elapsed from appearance of umbilicus until head delivered. Extended arm	A. C. H. F.*	Barely noticeable	1.6	7.08	1	$\frac{1}{20}$	8
2 Term	Head caught in uterine incision 2 to 4 minutes	Classical Cæsarean section	Very slow, but regular. Fair quality	5+ (Including mouth-to-mouth insufflation). No response. Condition desperate	$\frac{1}{20}$	9
3 Premature. 7½ mo.	Undetermined. Fetal heart sounds which had been strong and regular suddenly disappeared exactly 10 minutes before delivery	Mid-forceps	Imperceptible	0.8	7.02	1	$\frac{1}{20}$	7
4 Term	Undetermined	Spontaneous L.O.A.	Barely perceptible. Very slow and irregular	3.2	7.15	3-4 (Including mouth-to-mouth insufflation.) No response. Condition grave	$\frac{1}{20}$	10
5 Term	Premature separation of placenta	Low forceps	Slow and faint	2.8	7.12	3 No response	$\frac{1}{20}$	10
6 Term	Breech extraction	3.2	7.14	1	$\frac{1}{20}$	8
7 Term	3 loops of cord around neck. Fetal heart irregular for 3 hours before delivery. Very slow and faint for last half hour. Not heard during pains. Forceps extraction	Difficult mid-forceps	Very slow and faint (15 per minute)	0.6	7.02	5 Thorough suction. Clamp on tongue. Frequent slapping. Mouth-to-mouth insufflation. (3 attempts.) Artificial respiration by pressure on chest and abdomen with inhalator over mouth and nose. (Rhythmic compression of inhalator bag.) No response	$\frac{1}{20}$	9

* A.C.H.F.—after coming head, forceps.

OF TEN NEWBORN INFANTS SUFFERING FROM ASPHYXIA PALLIDA.

	Elapsed time from tripping to first inspiration (seconds)	Response	Auxiliary measures	Approximate interval before rhythmic breathing	Subsequent treatment	Last observation
10	8	Slight stiffening of arms. Marked opisthotonus. Faint gasp, short apnoea, two more weak gasps, short apnoea, numerous irregular respirations	Heat. Traction on tongue with clamp. Inhalator after third gasp. (CO ₂ 7%—O ₂ 93%)	2 hours	Inhalations of CO ₂ 7%—O ₂ 93% 5 minutes twice daily for 5 days	13th day normal
20	9	Marked stiffening. Irregular sudden inspirations with unco-ordinated movements of head and neck	Heat. Pure O ₂ from funnel for 5 minutes after respirations initiated	30 minutes	None	12th day normal
20	7	Slight stiffening entire body. Weak gasp followed by shallow, irregular respirations quickly improving in depth and regularity. Immediate improvement in colour	Heat only	40 minutes	Inhalations of CO ₂ 5%—O ₂ 95% 5 minutes twice daily for 8 days	24th day normal
20	10	Slight opisthotonus. Deep vigorous inspiration followed by apnoea for 30 seconds, then irregular but adequate respirations	Heat. Inhalator after respirations established	30 minutes	None	12th day normal
20	10	Vigorous inspiration. Rapid deep respirations with heaving of chest and abdomen	None	15 minutes	None	12th day normal
20	8	Gasp and frequent deep respirations	Oxygen by funnel for several minutes after respirations commenced	15 minutes	None	11th day normal
20	9	After failure of previous methods, intravenous therapy attempted. Cord short and vessels collapsed. Reverse stripping permitted successful injection. Milked into general circulation. Death was imminent. Very slight increase of tonus followed by weak gasp. Short apnoea, then weak, irregular respirations. These improved slowly when inhalator re-applied	Heat. Inhalations of CO ₂ 7%—O ₂ 93% for 30 minutes	12 hours	CO ₂ 7%—O ₂ 93% 5 minutes every 2 hours for 24 hours. 5 minutes twice daily for 8 days. Whiskey. Strychnine	13th day normal

TABLE I (Continued).—SUMMARY OF THE IMPORTANT FACTS CONCERNING THE RESUSCITATION

Infant	Cause of asphyxia	Delivery	Cardiac impulse	Oxygen content (volumes per cent.)	pH	Simple measures of resuscitation (minutes)	Dose of lobeline (grains)
8 Term	Breech extraction. Impacted shoulders. Extended arms	...	Slow and weak	3.6	7.20	2-3 No response	$\frac{1}{16}$
9 Term	Difficult breech extraction	A.C.H.F.*	Imperceptible	1.0	7.06	1-2 No response	$\frac{1}{16}$
10 Term	Long dry labour. Cord tight around neck	Difficult low forceps	Slow, faint and irregular	0.8	7.08	4 + Including traction on tongue and artificial respiration with inhalator over mouth and nose. No response. Pallor increased and heart action became more feeble. Combination technique then employed. A total of from 8-10 minutes elapsed before cord was stripped. Sound in position in trachea. Prognosis doubtful	$\frac{1}{16}$

Average oxygen content ... 1.955 volumes per cent

Average pH ... 7.096

* A.C.H.F.—after coming head, forceps.

OF TEN NEWBORN INFANTS SUFFERING FROM ASPHYXIA PALLIDA.

Elapsed time from stripping to first inspiration (seconds)	Response	Auxiliary measures	Approximate interval before rhythmic breathing	Subsequent treatment	Last observation
Less than 10	Deep inspiration followed by deep irregular respirations	Continuous O ₂ by funnel. Spinal tap	Died after 22 hours. Cerebral hæmorrhage with tentorial tear. Autopsy
6-7	Stiffening of body. Weak gasp followed by several shallow respirations. Sudden improvement in colour and deepening of respirations. Latter became laboured just before withdrawal of tracheal sound. Cardiac impulse rapid and strong. Complete restoration of tonus	Tracheal sound (Flagg). CO ₂ 20%—O ₂ 80% intermittently for ½ minute. (5 mm. mercury.) Cord then stripped. Above continued for 1 minute after initial gasp. Sound withdrawn and inhalator applied. CO ₂ 7% — O ₂ 93% for 5 minutes. Repeated 15 minutes later. (Combination technique)	90 minutes	Inhalations of CO ₂ 7% — O ₂ 93% 5 minutes twice daily for 5 days	12th day normal except for fractured clavicle
6	Marked stiffening of body and mild opisthotonus. Deep inspiration with moderate period of apnoea. Several double inspirations and then respirations of increasing vigour, depth and frequency. Removal of sound followed by irregular sighing movements. With inhalator in place improvement was progressive	(Combination technique.) Similar to preceding case except inhalator used for 15 minutes	Several hours	Inhalations of CO ₂ 7% — O ₂ 93% 5 minutes twice daily for 3 days	14th day normal

TABLE II.*—RESPIRATORY DEPRESSION OCCURRING IN 17,860 LIVE-BIRTHS, INCLUDING 1,051 PREMATURES.

Mild asphyxia	78
Moderate asphyxia	215
Severe asphyxia (including asphyxia pallida)	88
Total number which did not breathe promptly at birth	381—2.13%
Respirations initiated or re-initiated by intravenous therapy	234
Mild asphyxia	23
Moderate asphyxia	143
Severe asphyxia (including asphyxia pallida)	68
DEATHS (failure to respond or response followed by death within two weeks)	23
Asphyxia and congenital malformations	2
Asphyxia and hæmorrhagic disease	1
Asphyxia and cerebral hæmorrhage	6
Asphyxia	4
Asphyxia, atelectasis and prematurity	10

Prematures of less than twenty-eight weeks' gestation are omitted. Also all dead-born. The absence of visible or audible cardiac pulsations was the principal criterion in cases of doubt. The majority of doubtful cases received an injection of epinephrin directly into the heart. On rare occasions a response was obtained, the case then being treated and classified as a live-birth.

* Statistics compiled by Dr. Martin Z. Glynn.

method, it would seem that there is something to be gained and nothing to be lost by its use. The answer is decidedly in the affirmative if a prolonged apnoea which has not responded to simple measures must be treated. This procedure will often initiate respiratory movements which, even if irregular, and comparatively few in number, result in air entering the alveoli. Although this only fulfils part of our recommendation, it is superior to crude, older methods.

Unless each stage of a technique has been previously experienced, success will not necessarily attend the first use of modern methods in an urgent case. Adeptness at identifying, injecting and stripping the umbilical vein is gained by injecting saline into normal infants. It has been observed that a primary failure will often severely prejudice one against later attempts, even when the technique was faulty.

We sincerely feel that a consideration of this study by those with open minds will result in the saving of many lives which would otherwise be lost.

BIBLIOGRAPHY

- 1 BEHRENS, B., and PULEWKA, P., *Klin. Wehnschr.*, 1926, **37**, 1667.
- 2 BLAICKLEY, J. B., and GIBBERD, G. F., *Lancet*, 1935 (i), 737.
- 3 BRICKLEY, Paris Letter, *J. A. M. A.*, 1935, **104**, 1836.
- 4 CORNISH, R. E., cited in "Lazarus, Dead and Alive", *Time*, 1934, **23**, 49.
- 5 CORYLLOS, P. N., and BIRNBAUM, G. L., *Arch. Surg.*, 1929, **19**, 1346-1423.
- 6 CURTIS, F. R., and WRIGHT, S., *Lancet*, 1926 (ii), 1255.
- 7 DE LEE, J. B., "The Principles and Practice of Obstetrics", Philadelphia, 1927.
- 8 DOLLINGER, K. V., *Gas- u. Wasserfach*, 1926, **69**, 561.
- 9 EASTMAN, N. J., *Bull. Johns Hopkins Hosp.*, 1932, **50**, 39-50.
- 10 ECKSTEIN, A., ROMINGER, E., and WIELAND, H., *Ztschr. f. Kinderh.*, 1921, **28**, 218.
- 11 EDMUNDS, C. W., *Am. J. Physiol.*, 1904, **11**, 79.
- 12 EVE, F. C., *Lancet*, 1932 (ii), 995; KILICK, E. M., and EVE, F. C., *Lancet*, 1933 (ii), 740.
- 13 FLAGG, P. J., *J. A. M. A.*, 1928, **91**, 788; *Am. J. Obst. and Gynec.*, 1931, **21**, 537.
- 14 HENDERSON, Y., HAGGARD, H. W., and COBURN, R. C., *J. A. M. A.*, 1920, **74**, 783.
- 15 HENDERSON, Y., Personal Communication.
- 16 HOLTMANN, N., *Klin. Wehnschr.*, 1925, **4**, 2346.
- 17 IRVING, F. C., BERMAN, S., and NELSON, H. B., *Surg., Gynec. and Obst.*, 1934, **58**, 1-11.
- 18 KING, M. J., HOSMER, H. R., and DRESBACH, M., *J. Pharmacol. and Exper. Therap.*, 1928, **32**, 241.
- 19 KREISELMAN, J., KANE, H. F., and SWOPE, R. B., *Am. J. Obst. and Gynec.*, 1928, **15**, 552.
- 20 LANG, O., *Ztschr. f. Gynäk.*, 1926, **23**, 1465.
- 21 LEFF, M., *Am. J. Obst. and Gynec.*, 1932, **24**, 898.
- 22 MENNET, J., *Ztschr. f. Gynäk.*, 1926, **23**, 1522.
- 23 MONCRIEFF, ALAN, *Lancet*, 1935 (i), 664-669.
- 24 MURPHY, D. P., and BAUER, J. T., *Am. J. Dis. Child.*, 1933, **45**, 1196-1202.
- 25 MURPHY, D. P., and SESSUMS, J. V., *Surg., Gynec. and Obst.*, 1932, **55**, 432-439.
- 26 MURPHY, D. P., WILSON, R. B., and BOWMAN, J. E., *Am. J. Obst. and Gynec.*, 1931, **21**, 528-536.
- 27 MUTO, K., and IWAKAWA, K., *Arch. f. exper. Path. u. Pharmacol.*, 1910, **62**, 282.
- 28 NORRIS, V. H., and WEISS, S., *J. Pharmacol. and Exper. Therap.*, 1927, **31**, 43.
- 29 PIPER, E. B., *Gas Therapist*, 1934, **1**, 15.
- 30 SCHMIDT, CARL F., *Am. J. Physiol.*, 1928, **84**, 202.
- 31 SCHOEN, R., and KAUBISCH, N., *Deutsches. Arch. f. klin. Med.*, 1926, **150**, 251.
- 32 SCHUMACHER, P., *Ztschr. f. Geburtsh. u. Gynäk.*, 1924, **88**, 151.
- 33 SCHWARTZ, A., *Compt. rend. Soc. de Biol.*, 1926, **95**, 693.
- 34 WALBAUM, H., *Arch. f. exper. Path. u. Pharmacol.*, 1926, **116**, 1.
- 35 WIELAND, H., *Arch. f. exper. Path. u. Pharmacol.*, 1915, **79**, 95.
- 36 WIELAND, H., and BEHRENS, B., *Ztschr. f. d. ges. exper. Med.*, 1927, **56**, 454.
- 37 WIELAND, H., and MAYER, R., *Arch. f. exper. Path. u. Pharmacol.*, 1922, **92**, 195.
- 38 WIELAND, H., SCHOEPP, C., and HERMSEN, W., *Ann. d. Chem.*, 1925, **444**, 740.
- 39 WILSON, R. A., *Am. J. Obst. and Gynec.*, 1928, **16**, 379.
- 40 WILSON, R. A., and TORREY, M. A., *Am. J. Surg.*, 1934, **23**, 426-437.

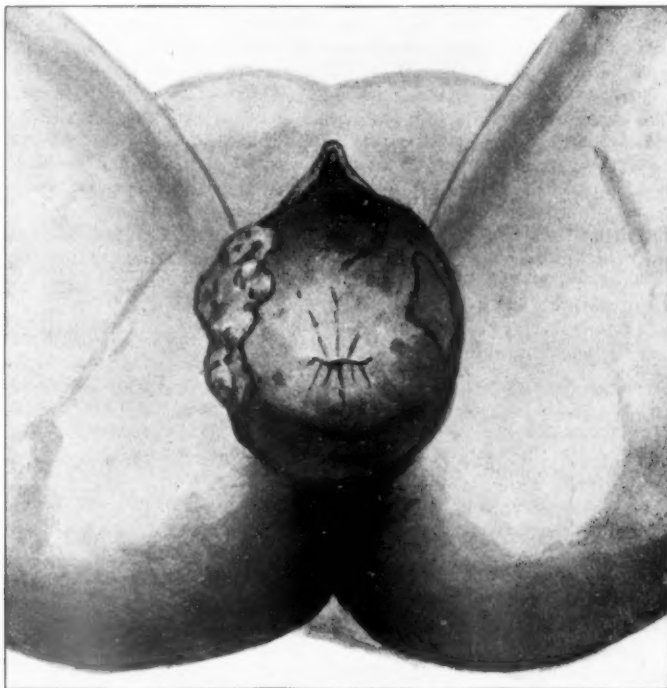
[June 18, 1937]

Carcinoma of the Vagina Complicating a Complete Procidentia

By M. BASDEN, F.R.C.S.

THE specimen that I am showing consists of a uterus and vagina removed by vaginal hysterectomy for complete procidentia complicated by carcinoma of the vagina, and I thought it might be of some interest, owing to its comparative rarity.

The malignant ulcer measured $2\frac{1}{2}$ by $1\frac{1}{2}$ in., and was on the right side of the prolapse, and in addition there was a simple ulcer on the left side measuring $2\frac{1}{2}$ by 2 in. There was also a small very superficial ulcer at the base of the right labium majus where it was in contact with the carcinoma. Microscopic examination of



this small ulcer showed that it was innocent. The cervix was very atrophic and difficult to locate; otherwise it was normal.

The patient was a woman of 69, but she looked much older, and was very fragile. She was admitted under my care to the South London Hospital in September 1936, with a history that she had had a lump coming down for thirty-eight years, and that for the last two months it had been associated with a blood-stained discharge. She was in a very miserable condition, and complained of a

[I am indebted for some excellent illustrations, one of which is reproduced above, to my anaesthetist, Dr. Freda Allport.]

dragging pain near the umbilicus, and great difficulty in sitting. She said she had worn a ring pessary many years ago, but that as far as she could remember she had abandoned it in 1919, having found it useless. She had had six children, the youngest of whom was aged 38.

I did a vaginal hysterectomy and repaired the prolapse. I also removed the right labium majus, in case the ulcer in contact with the growth might be undergoing malignant degeneration. I was afraid to do more, or to remove the inguinal glands, owing to her very poor condition. She made a good recovery, and was discharged from hospital about three and a half weeks after the operation. I have seen her from time to time since; her general condition has greatly improved, and she says she has never felt so well before. I have tried to persuade her to have the inguinal glands removed, but she refuses to have any further operation.

Professor Beckwith Whitehouse has an illustration of a case almost exactly like my own in the new edition of Eden and Lockyer's "Gynæcology". The predisposing causes of primary vaginal carcinoma are there given as a neglected pessary, and prolapse, and it thus differs from carcinoma of the cervix in which prolapse seems to play little or no part in the ætiology. At the Marie Curie Hospital, among about 1,600 cases of carcinoma of the female genital tract treated during the last twelve years there were several cases of complete procidentia associated with carcinoma of the fundus, but only two with cervical carcinoma. Of the less severe degrees of prolapse I have no record. There were 18 cases of primary carcinoma of the vagina, of which one was associated with complete procidentia.

In reference to the cervix cases at the Marie Curie Hospital complicated by procidentia, it is interesting to note that in one of them, the radium employed to treat the carcinoma not only cured the growth but cured the prolapse too, by the resulting contraction.

I did not know of this possible alternative method of dealing with prolapse when I operated on the case just reported.

Mr. A. V. CLEMMY said that, working in East Africa, he had seen two cases of cancer of the cervix uteri with complete procidentia in native women. In both there had been glandular involvement; in only one a histological examination was made and the diagnosis confirmed, but he had no doubt of the condition of the other in which the patient was almost moribund when she first attended.

Section of Otology and Section of Laryngology COMBINED MEETING

HELD AT NORWICH, JUNE 18 and 19, 1937

OTOLOGICAL SESSION

Chairman—DOUGLAS GUTHRIE, M.D. (President of the Section of Otology)

Some Problems of Aural Medicine

By S. H. MYGIND and DIDA DEDERDING (Copenhagen)

THE term "aural medicine" may sound a little strange to a generation of otologists who have been proud of regarding themselves principally as "aural surgeons". Wilde, more than eighty years ago, named his famous book "Aural Surgery", and "to rescue aural surgery from the hands of quacks" was the noble aim of Toynbee, one of the founders of modern otology, though certainly not what we would nowadays call an aural surgeon. Later came the period of surgical victories gained by Schwartze and his followers, victories so brilliant that we have now in some degree forgotten to pay sufficient attention to the problems of aural medicine. How many remember, for instance, a great Frenchman called Itard, whose "Manual of Otology", published in 1820-21, is a mine of information, even to the modern reader, abounding with fresh and ingenious observations showing the intimate relation between the ear and the general condition of the body, and the effect on the ear produced by general influences and by general treatment.

We must confess that the treatment of the non-surgical diseases of the ear has not reached very far beyond the catheterization of the Eustachian tube devised by the old Versailles postmaster nearly two hundred years ago. This is due principally to the dramatic and engrossing evolution of aural surgery but partly, we think, to a somewhat erroneous conception of the localization and nature of a series of non-suppurative ear diseases.

The researches of one of us (D. D.) have shown that our interpretation of the findings by the acoustic tests need revision.

TABLE I.—PURE PERCEPTION AFFECTION.

Upper limit air-conduct.	Lower limit	a ₁ Air (norm. 70°)	a ₁ Bone (norm. 20°)	Whisper	Convers.
600 dbl. vibr.	16 dbl. vibr.	19"	5½"	0.40 m.	1.50 m.
0 dbl. vibr.	0 dbl. vibr.	6"	0"	0 m.	0 m.

We have learned that perception deafness is characterized by a lowering of the upper limit. But this holds good only if there is a lowering, not only by air-conduction, but also by bone-conduction (Table I). We have likewise learned that a disturbance

of sound perception is accompanied by an abridged bone-conduction. This is only true if the bone-conduction is reduced in exactly the same proportion as the air-conduction. Sound perception affection is further characterized by the lower limit always keeping normal (except in very advanced cases). The hearing of the high-pitched whispered voice is, naturally, comparatively more severely impaired than the hearing of the low-pitched conversation voice.

On the other hand, sound-conducting deafness is characterized, in the first place, by an elevation of the lower limit, whereas the upper limit in not too pronounced cases is preserved. In severe cases, however, it lowers the upper limit, though only by air-conduction; by bone-conduction it always remains normal. This was substantiated by a series of cases of typical sound-conducting deafness. To avoid the disturbing influence of transfer by bone-conduction to the better hearing ear, only cases with equal hearing on both sides or with complete deafness on one side were included.

This is seen in otosclerosis (Table II), after radical mastoid operations (Table III), and the sequelæ of chronic suppuration (Table IV).

Even a plug of earwax may give the same lowering of upper limit by air-conduction (Table V). The double testing of the upper limit by air and by bone therefore becomes our best method of distinguishing between a sound-conducting and a sound-perceiving affection. Air- and bone-conduction may be reduced in exactly the same proportion though an alteration of this proportion is much more frequent; either the bone-conduction is absolutely, or only relatively, longer than air-conduction. The variation may be in the opposite direction, so that bone-conduction in relation to air-conduction is reduced or absent.

TABLE II.—OTOSCLEROSIS (3 OUT OF 32 CASES).

Age. Years	Duration of disease. Years	Upper limit air-conduct.	Upper limit bone-conduct.	Lower limit	Rinne	a ₁ Air (norm. 76")	a ₁ Bone (norm. 22")	Whisper	Convers.
37	17	6000 dbl. vibr.	17000 dbl. vibr.	> 150	÷	0"	6"	0 m.	ad aurem
		8000 dbl. vibr.	17000 dbl. vibr.	> 150	÷	9"	7"	0 m.	0.10 m.
46	21	÷ Monochord	15000 dbl. vibr.	> 150	÷	14"	22"	0 m.	0.30 m.
		÷ Monochord	15000 dbl. vibr.	> 150	÷	15"	23"	0 m.	0.30 m.
71	57	÷ Monochord	14000 dbl. vibr.	> 150	÷	0"	6"	0 m.	ad aurem
		÷ Monochord	14000 dbl. vibr.	> 150	÷	0"	5"	0 m.	ad aurem

TABLE III.—RADICAL OPERATIONS (DRY CAVITIES. 3 OUT OF 11 CASES).

Age. Years	Upper limit air-conduct.	Upper limit bone-conduct.	Lower limit	a ₁ Air (norm. 69")	a ₁ Bone (norm. 16")	Whisper	Convers.	
43	11000 dbl. vibr.	15000 dbl. vibr.	90 dbl. vibr.	19"	17"	0.20 m.	14.00 m.	
	11000 dbl. vibr.	15000 dbl. vibr.	150 dbl. vibr.	14"	18"	0.10 m.	14.00 m.	
25	6000 dbl. vibr.	16000 dbl. vibr.	90 dbl. vibr.	11"	17"	0.30 m.	3.00 m.	(÷ Ac. ÷ Vest. Reaction)
	0 dbl. vibr.	0 dbl. vibr.	0 dbl. vibr.	0"	0"	0 m.	0 m.	
39	9000 dbl. vibr.	17000 dbl. vibr.	90 dbl. vibr.	16"	17"	0.10 m.	4.00 m.	
	9000 dbl. vibr.	17000 dbl. vibr.	90 dbl. vibr.	16"	17"	0.30 m.	4.00 m.	

TABLE IV.—SEQUELÆ OF CHRONIC SUPPURATIVE OTITIS MEDIA.
(Dry Cavities. 3 out of 38 Cases.)

Duration of Age, disease. Years Years	Otoscopy	Upper limit Air-conduct.	Upper limit Bone-conduct.	Lower limit	a ₁ Air (norm. 70")	a ₁ Bone (norm. 20") Rinne	Whisper	Convers.
45	25	Scar	11000 dbl. vibr.	19000 dbl. vibr.	36 dbl. vibr.	16"	21" ÷	ad aurem 1-00 m.
		Scar	11000 dbl. vibr.	20000 dbl. vibr.	50 dbl. vibr.	21"	22" ÷	ad aurem 0-80 m.
38	37	Scar	8000 dbl. vibr.	15500 dbl. vibr.	> 150 dbl. vibr.	0"	3" ÷	0 m. 0-30 m.
		Scar	8000 dbl. vibr.	17000 dbl. vibr.	> 150 dbl. vibr.	0"	4½" ÷	0 m. 0-10 m.
73	> 60	Scar	< 6000 dbl. vibr.	15000 dbl. vibr.	60-80 dbl. vibr.	22"	11"	0 m. 0-50 m.
		Scar	< 6000 dbl. vibr.	14000 dbl. vibr.	60 dbl. vibr.	34"	13"	0 m. 0-50 m.

TABLE V.—CERUMEN IN THE RIGHT EAR.

<i>Before removal.</i>					
Upper limit Air-conduct.	Upper limit Bone-conduct.	Lower limit	a ₁ Air (norm. 60")	a ₁ Bone (norm. 20")	Whisper
10000 dbl. vibr.	17000 dbl. vibr.	90 dbl. vibr.	21"	18"	1-50 m.
15000 dbl. vibr.	17000 dbl. vibr.	16 dbl. vibr.	60"	20"	20-00 m.
<i>After removal.</i>					
15000 dbl. vibr.	17000 dbl. vibr.	16 dbl. vibr.	60"	20"	20-00 m.
15000 dbl. vibr.	17000 dbl. vibr.	16 dbl. vibr.	60"	20"	20-00 m.

In 721 cases of non-suppurative deafness the findings were as follows :—

TABLE VI.—721 CASES OF NON-SUPPURATIVE HARD HEARING.

Upper Limit tested by Bone- and Air-Conduction.

Sound-conducting affection	640 (89%)
Sound-perceiving affection	24 (3%)
Sound-conducting + sound-perceiving affection ...	57 (8%)

The majority of cases of deafness of syphilitic and traumatic origin are in this way found to belong to the sound-conducting type.

TABLE VII.—SYPHILIS. (WASSERMANN REACTION +. 3 OUT OF 39 CASES.)

Age. Years	Upper limit Air-conduct.	Upper limit Bone-conduct.	Lower limit	a ₁ Air (norm. 70")	a ₁ Bone (norm. 20")	Whisper	Convers.
37	9000 dbl. vibr.	16000 dbl. vibr.	38 dbl. vibr.	norm. 15"	18"	ad aurem	3-00 m.
	7000 dbl. vibr.	16000 dbl. vibr.	75 dbl. vibr.	70" 42"	14"	0-50 m.	6-00 m.
47	10000 dbl. vibr.	14000 dbl. vibr.	36 dbl. vibr.	norm. 25"	15"		20-00 m.
	11000 dbl. vibr.	14000 dbl. vibr.	38 dbl. vibr.	60" 40"	15"		20-00 m.
62	6000 dbl. vibr.	14000 dbl. vibr.	50 dbl. vibr.	norm. 13"	7"	0 m.	2-00 m.
	6000 dbl. vibr.	14000 dbl. vibr.	45 dbl. vibr.	70" 15"	8"	ad aurem	3-00 m.

Our investigation has further taught us that in reality there is no sharp line of separation between affections of the middle ear and affections of the labyrinth. If we examine such cases which are generally termed neuro-labyrinthitis, we find the cochlear nerve quite intact, as is evidenced by the well-preserved upper limit. The labyrinth certainly is affected, as is demonstrated by vestibular phenomena and frequent tinnitus, but the lesion is localized peripherally to the organ of perception itself. On the other hand, the middle ear also is involved in the pathological process, as appears from the very common otoscopic changes and the rather frequent tubal stenoses. The sound-conducting type of deafness suggests that also in these cases we have to deal with a fixation of the stapes by changes which may be situated on either its inner or its outer side, whether in the labyrinth or in the middle ear.

On the other hand, many cases of apparently ordinary tubal stenosis, or so-called middle-ear catarrh, are accompanied by labyrinth phenomena in the form not only of tinnitus but also of vertigo and nystagmus. Unfortunately a common and appropriate term (? otosis) for all these clinically varying, but really identical, conditions does not exist. When the vestibular symptoms are particularly marked and of paroxysmal occurrence, we speak of Ménière's disease.

In Ménière's disease, however, it is not only the vestibular function which fluctuates but the acoustic function also. At the same time there are fluctuations in the general condition of the body. The study of Ménière's disease thus becomes a problem not only of otology but also of general medicine.

This characteristic fluctuation, particularly the fluctuation of hearing, which can be accurately tested, affords an excellent opportunity of studying the interrelation between the different phenomena and the factors which give rise to the change from one side to the other.

After a series of clinical observations and experiments we have come to the conclusion that, both in Ménière's disease and in many other sound-conducting affections, we have to deal with a disturbance of the vascular function, especially in the capillaries, both in the ear itself and in other parts of the body.

This general capillary deficiency manifests itself by a series of vasomotor symptoms, such as acrocyanosis, chilliness, vasomotor rhinitis, &c.—symptoms which are particularly pronounced during bad periods when the patient's hearing is poor. Such bad periods are often due to cold or infections or exhaustion, by which the capillaries are paralysed. This may be seen, for instance, in cases of angina or influenza; in reality it is also what takes place in syphilis, which is known to have a particularly toxic influence on the vessels.

The result of this deficiency of capillary function is a dropsical swelling of the insufficiently nourished cells themselves, an intracellular oedema, which must be distinguished from the ordinary nephritic or cardiac inter- or extra-cellular oedema, in which the accumulation of fluid takes place in the intercellular spaces.

In the middle ear such oedematous processes result in a condition which is presumably identical with the persisting foetal type of mucous membrane, described by Wittmaack as leading to restrained pneumatization. An extracellular oedema in the labyrinth gives rise to an increase of the intralabyrinthine pressure, with nystagmus and giddiness, besides a reduction of hearing of the sound-conducting type, owing to the fixation of the stapes. Consequently, a fluctuation of hearing will ensue in accordance with the slightest alteration in the pathological condition. The vascular disturbances and the oedema may disappear and the hearing may be entirely restored, but if the deleterious influences are of sufficiently long duration, secondary unalterable processes, especially of fibrous and atrophic character, may develop, and are partly to be seen, by otoscopy, in the drum. This condition is probably identical with the fibrous type of mucous membrane of the middle ear, described by Wittmaack. The final result is a fixation of the stapes and an incurable deafness. According to the function tests, only the perception apparatus seems to resist to the very last.

All over the body, wherever there is a weak spot, the same influences bring about the same capillary deficiency and lead to the same intracellular oedema. The oedema in the brain, or, rather, perhaps, in its membranes, gives rise to headache, which is generally most violent on the same side as the deafness. In the nose a vasomotor rhinitis develops, and in the alimentary tract the same cedematous process is responsible for the frequent associated dyspeptic symptoms. The frequent rheumatic symptoms may be explained by corresponding and partly palpable "infiltrations" in muscles, tendons, and joints. The so-called subcutaneous infiltrations are of the same nature.

Thus we have to deal with a tendency to the accumulation of water in the whole body, i.e. a disturbance of the general water metabolism. Therefore we find that these patients, during the bad periods when their hearing becomes weaker, often increase in weight and have only a scanty output of urine, whereas, during the periods of improvement they lose in weight and have a copious discharge of urine.

We have been able to substantiate these clinical observations by adequate clinical experiments. Dehydration may be brought about in many different ways but, whether we employ the old pilocarpine perspiration treatment of Politzer, a thirst cure, or any kind of diuretic, the same improvement of hearing may, in suitable cases, be obtained when the patient loses in weight and becomes thirsty. This is evidenced by one of our experiments with salyrgan (Table VIII).

TABLE VIII.—SALYRGAN EXPERIMENT.

	Weight	Upper limit (air)	Lower limit	a ₁ Air (norm. 60")	a ₁ Bone (norm. 15")	Whisper
Before injection	78.6	8000 dbl. vibr.	18 dbl. vibr.	22"	6"	2.00 m.
		8000 dbl. vibr.	18 dbl. vibr.	18"	10"	0.75 m.
6 h. after injection	78.0	8000 dbl. vibr.	18 dbl. vibr.	24"	8"	2.00 m.
		8000 dbl. vibr.	18 dbl. vibr.	45"	11"	2.00 m.
27 h. after injection	77.7	8500 dbl. vibr.	20 dbl. vibr.	26"	9"	2.00 m.
		8500 dbl. vibr.	18 dbl. vibr.	41"	10"	2.00 m.
45 h. after injection	77.5	9500 dbl. vibr.	15 dbl. vibr.	38"	8"	4.00 m.
		9000 dbl. vibr.	15 dbl. vibr.	48"	11"	6.0-10.0 m.

On the other hand, by a simple water test, in which the patient is caused to drink between 800 and 1,000 c.c. of water, the opposite effect may be produced, as is seen from the accompanying graph (see Table IX, p. 80). The hearing is reduced and, in some cases, an additional spontaneous nystagmus or even a feeling of pressure in the ear occurs, but whether our experiments lead to an improvement or to a reduction of hearing, the changes are always of pure sound-conducting type.

The correctness of the results of these experiments has been corroborated by Fürstenberg in U.S.A., though apparently only partially, as he came to the conclusion that a surplus not of water, but of salt, is the essential factor. Fürstenberg's experiments have been conducted with the greatest possible exactness as regards weighing and measuring of intake and output. He, however, only examined the spontaneous nystagmus and not the hearing of the patients. And as a nystagmus may accompany either a rise or a fall in hearing, we cannot wonder that he obtained a spontaneous nystagmus by giving salt alone, as we ourselves have produced a temporary rise of hearing in this way. The patients become thirsty, and water is temporarily withdrawn from the tissues into the blood.

A part of the water is probably retained in the so-called subcutaneous infiltrations. These, as said above, are very frequently met with in such patients, not only in females—in whom they may usually be found—but also in males. They are particularly pronounced and very tender during bad periods. As they depend on the state of the capillaries, they are preferably found in places where the circulation is poor. This is demonstrated by the coolness, paleness, or cyanosis, of the covering skin, where often the capillary reflexes are deficient also. The influence of circulation on the subcutaneous infiltrations is evidenced by their dependence on the hydrostatic pressure. This is the reason of their being so severe in the lower parts of the body, for instance in the legs, where they are more pronounced in the evening than in the morning, owing to the erect posture in the day. Conversely in the morning, when the head has been kept low during the night, the patient may present a swelling of the skin of the face, which disappears in the course of the day. Several other cephalic phenomena present the same postural relation to the hydrostatic pressure. We all know people who in the morning complain of headache, indisposition, or obstruction of the nose, and who

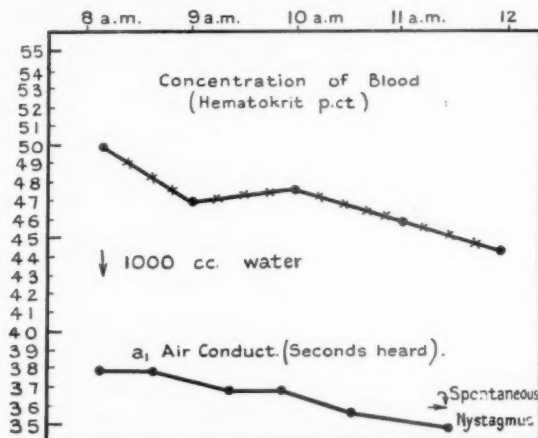


TABLE IX.

feel perfectly well later in the day. The same morning oedema is present in the ear. Itard described such patients whose hearing on going to bed in the evening is good, and who next morning, especially after a long and sound sleep, wake up stone deaf.

As the accumulation of water takes place in the cells themselves and not in the intercellular spaces, the subcutaneous infiltrations, in contradistinction to the oedema attending nephritis and heart failure, do not leave any marks of finger pressure.

As will be understood, it is these directly visible and palpable subcutaneous infiltrations which have given the clue to the underlying pathological alterations in the ear and elsewhere. In reality we must admit that we know very little about intracellular oedema. The microscopic pictures of subcutaneous infiltrations apparently do not differ from those of ordinary subcutaneous tissue. Albert Gray had found nothing abnormal on microscopy of the labyrinth of a Ménière patient who had been clinically examined by Berggren. Probably the pathological alterations in question are so faint and transient that they disappear in our ordinary preparations.

Certain experiments, which Professor Péterfi has been kind enough to carry out for us, seem, however, to support our hypothesis. Living amoebæ placed in a hypo-

tonic solution will swell to a certain degree. If, instead of quite fresh specimens, the amœbæ have for some time been kept in the same nourishing substrate, the swelling in the hypotonic solution will be much more marked; by the poor nutrition their resistance against œdematization seems to have been reduced. A similar reduction of resistance or an increase of permeability may be observed in old amœbæ. It can also be produced by injuring the amœbæ with a fine needle. This experiment has also been performed with a tissue culture of fibroblasts, in which the injured cell in a hypotonic solution is seen to swell much more than the neighbouring cells.

According to our hypothesis, which implies that the intracellular œdema is essentially due to an impairment of the respiratory metabolism in the cells on account of capillary inefficiency, we endeavoured to suffocate a fibroblast culture with carbonic acid. The carbonic acid does not seem to exert much influence on the cells, but if these are subsequently placed in a strong hypotonic solution, such as for instance distilled water, they will swell much more than a culture not previously treated with carbonic acid. One is tempted to suppose that it is one and the same process which takes place in this experiment and in the human body, and thus gives rise to an intracellular œdema in the ear, or in other parts of the body, where it manifests itself most evidently in the subcutaneous infiltrations.

Further support of this hypothesis is afforded by experiments recently carried out by Falbe-Hansen, who succeeded in poisoning guinea-pigs by large subcutaneous injections of water and subsequent microscopic demonstration of a swelling or intracellular œdema in the labyrinth, particularly in the epithelium of Corti. The swelling is particularly seen in the hair-cells which are much broader than in the normal preparation.

We are far from considering that our investigation of these subjects is terminated, and we are quite aware that we may be compelled to modify our views in many respects. What we wanted to show to-day are the principal features of an attempt at uniting a series of clinical, anatomical, and physiological phenomena in a simple system of explanation applicable not only to the ear but to every other part of the body, where a hereditary predisposition, a previous inflammation, a traumatic lesion, or an accidental structural weakness has conditioned a *locus minoris resistentiæ*. Whatever the primary causes may be, the essential part of the mechanism of origin is a vascular—and, particularly, a vasomotor—deficiency, leading to a local or more or less universal intracellular œdema. The reason why the result of these processes is clinically much more conspicuous in the ear than elsewhere in the body, is that the labyrinth is a sensory organ with a double and very sensitive function, in which the sensory epithelial cells have a delicate osmotic regulation, necessary for the maintenance of their function in the easily influenced surrounding of fluid. The slightest disturbance of this regulation leads to a swelling of the sensory epithelium resulting in an increase of the content of the labyrinth and of the endolabyrinthine pressure. In the closed, unyielding, hydrostatic system of the labyrinth this increase of pressure immediately elicits acoustic—and, also, very often vestibular—phenomena. The pressure on the foot-plate provokes a deafness of the sound-conducting type, the slightest changes in which are detected by our functional tests.

It may be thought that we have gone beyond our otological domain and have lost ourselves too much in hypotheses. The starting-point, however, has been the clinic, and the object has been to find paths to the understanding and treatment of our patients. Upon the base of our observations, experiments, and theoretical considerations, we have built up a treatment which has afterwards been practically tried.

The first condition for a proper treatment is a thorough examination, taking into consideration the individuality of the single case, and the daily habits and the surroundings of the patient. In every case the particular cause—or rather combination of causes—has to be sought for and, if possible, eliminated. It will therefore often

be advisable to watch the patient in a hospital or clinic. Besides the ordinary medical and otological examination, a water test is carried out in order to determine any eventual retention of water. The general treatment consists principally in dehydration and in stimulation of the vasomotor function throughout the body. As a rule drugs are avoided; they may give momentary and considerable relief—as is the case with diuretics and pilocarpine—but, in the long run, they may be injurious. A thirst cure is carried out with from 500 to 800 gm. of fluid per diem, according to the individual tendency to water retention, to the climate, and to individual weight and work. We use a diet with very little salt but not entirely saltless. The food is cooked in the usual way, but no salt is allowed on the table, and particularly salt dishes (e.g. soup, cheese, bacon, sausages, canned food, &c.) are specially forbidden. In the quantity of fluid allowed we include that in fruit, vegetables, &c. A suitable loss of fluid is ensured by regularly weighing the patient. In case of overweight the amount of calories in the diet is reduced. In case of underweight a surplus of butter and cream is given, and arsenic is prescribed.

By general stimulating treatment we endeavour to train the capillaries in the skin, muscles, and lungs to a higher capacity. Baths with Finsen light (carbon-arc) as constituting the best substitute for active sunlight are beneficial, as are further massage, gymnastics, and fresh air. Other baths may also be made use of. In the home, concentrated salt-water baths (5 to 7 kilos salt per bath) with friction of the skin are recommended. The skin-tolerance of cold is helped forward by means of shower-baths at first tepid and later on cold—eventually in the form of the Scotch douche. In all treatments it is necessary to individualize and to advance step by step. A suitable mixture of rest and stimulation should be aimed at. A dry and warm climate is preferable. In cases of anæmia, iron—eventually together with arsenic—is given. For the climacteric, ovarian preparations may be necessary. Of these we prefer a German preparation, the "Klimacton" of Knoll, which contains also calcium-diuretine and a little thyreoidine. Ammonium chloride, 1 gm. three times a day, is often beneficial on account of its dehydrating influence, but it may cause nausea. When milk is taken away—as fluid and cheese—as containing too much salt, the calcium-content in the food may be dangerously reduced. In this, as also in other cases, we give calcium chloride 1 gm. three times a day. In the beginning of dehydration there is often increasing constipation, which must be treated with diet, paraffin oil, castor oil, cascara, and chamomilla clysmata.¹

The local treatment consists of daily catheterization of the Eustachian tube and looking out for eventual affections in nose, throat, and tonsils.

The results are controlled by regular examination not only of the vestibular but also of the acoustic function.

This treatment may, *mutatis mutandis*, be applied to many other affections, for instance, many cases of rheumatism, headache, indigestion, and tiredness. It is the same principle which lies behind the treatment of tuberculosis and the many different treatments with air, massage, gymnastics, and baths, known from the time of the Romans and still used at all the spas, helping thousands of patients suffering from many different diseases.

Thus the study of the problems here touched upon appears to lead to a better understanding not only of otological problems, but also of general medical problems and therefore also to rational treatment.

Discussion.—Dr. M. SOURDILLE (Nantes) said that this was most interesting work in respect of early changes in the ear, but in the main it was still largely a matter of hypothesis. He thought that at a later stage there developed, in many cases, secondary

¹ During the acute attack of giddiness it will generally be sufficient to keep the patient in bed. For very severe attacks we recommend injection of 0.6 mgm. of atropine sulphate, or ergotine preparation, 0.8 gm. in drops or solution. Of bulbocapnine recommended by Berggren we have no personal experience.

permanent changes, for which medical treatment could not be of avail. His experience had shown him that the changes in the labyrinth were secondary; often in middle-ear disease labyrinthine changes took place, and when the labyrinth was opened the hearing became normal. He asked whether Dr. Mygind had obtained results from his treatment in cases of deafness. He (the speaker) had tried to ascertain what was the pressure in the labyrinth when he opened it, but very little fluid had been present.

Mr. C. S. HALLPIKE said he gathered that Dr. Mygind thought it possible for an increase of pressure in the labyrinth to produce a conduction deafness. (Dr. Mygind: Yes.) Before accepting that, it would be necessary to consider what was the effect on hearing of an uncomplicated increase of pressure, about which a good deal was now known. MacNally and his collaborators had recently published a paper describing functional tests in cases of increased intracranial pressure, and, on the whole, there did not appear to be evidence that increased intracranial pressure, which must cause increased intralabyrinthine pressure, caused changes in the hearing.

Mr. THACKER NEVILLE said that he had gone to Copenhagen to study this question, and had seen a ward full of patients whom Dr. Mygind had cured. In many cases they had relapsed into their bad habits, but these Dr. Mygind rectified. Faulty water metabolism was not so common in England as in Denmark, but it was a mistake to treat vertigo by reducing the water intake and cutting out the salt, unless the water metabolism was first tested. It was torture to cut down the water to an extreme degree. He had had one case of a police-sergeant who sat in his office and drank tea practically all day, and was deaf and giddy. He (the speaker) had carried out the test described by Dr. Mygind, and after the patient had been given 1,000 c.c. of water he passed 500 c.c.; 300 c.c. were retained and the rest was not accounted for. He (Mr. Thacker Neville) had used the salyrgan treatment, but did not think it was of value except as a test. The patient mentioned had been restricted to a pint of tea daily, with slices of lemon to relieve his thirst, and he was now cured. In this country the people were poor beer-drinkers, and that was why they did not get water-logged. The late Dr. Albert Gray had spoken of vasomotor upset in otosclerosis, and, according to Dr. Mygind, the intracellular oedema was the important thing.

The paper showed extraordinary industry, and he thought Dr. Mygind was fortunate in having such an assistant as Dr. Dederding. Testing 721 patients represented enormous labour.

The CHAIRMAN asked Dr. Mygind to amplify his remarks on the Fürstenberg treatment. This treatment did not include limitation of fluid intake, and so was more acceptable to the patient.

Dr. MYGIND (in reply) said he could not understand why Americans had not found alterations in hearing in response to changes of intracranial pressure, because Dr. Dederding in many cases of brain tumour and other intracranial conditions had found an alteration in acuity of hearing. There, also, it was the sound-conducting type of defect. This led to the belief that such a case was one of ordinary middle-ear deafness. Following up such cases, however, showed that the hearing fluctuated with the intracranial pressure as manifested for instance by a changing choked disc. One should be careful about drawing conclusions from the Wever-Bray test. In America experiments had been made on dogs by plugging the round window, and it was found that when this was done the hearing tested by conditioned reflex became worse, not better as found by the Wever and Bray test.

He was glad to hear Mr. Thacker Neville's remarks about the salyrgan test, which he (the speaker) did not use as a treatment; indeed he used drugs as little as possible. But salyrgan could be used for diagnosing the oedema at the labyrinth in contra-distinction to an otosclerosis. The chief point was to choose the right patients. The patient should be kept on the edge of thirst, so that the tongue was just slightly moist. One must not expect to treat two cases exactly alike. He was grateful to Mr. Thacker Neville for his appreciation of Dr. Dederding's work; hundreds of patients had been treated, and nearly always the vertigo had been relieved, and in many the hearing was improved. But when secondary changes had set in and there was fixation of the ossicles, one could not expect to benefit the hearing.

The effect of the Fürstenberg diet lay in dehydration. This was increased by taking away not only the salt but also the water, and we did not know yet how the Fürstenberg diet acts on the hearing which was the principal proof.

Hearing and Speech in Deaf Children

By PHYLLIS MARGARET TOOKEY KERRIDGE, Ph.D., M.R.C.P.

Lecturer in Physiology, University College, London.

INTRODUCTION

A FEW years ago there was no satisfactory answer to the question "How deaf are the deaf?" to be found in otological literature. The work described in this paper was done in an attempt to provide an answer, at any rate in part. The inquiry has more than academic importance, because of the development of sound magnifying apparatus, and the need to assess the compensations which the deaf may gain thereby.

A convenient source of material for the investigation was the special schools in which children are educated when their handicap on account of deafness is sufficient to make it impossible for them to reap adequate educational benefit in the ordinary schools. No class of deaf persons needs more help, since many such children have been so severely deaf since birth or infancy that they have had to be taught to speak. This difficult and weary process deserves all the assistance that modern science can provide.

The research is described in full in a lengthy special report published recently by the Medical Research Council (No. 221, March, 1937), and the present paper deals shortly with some of the results which might interest otologists. The work can be considered in two parts. In the first place, the hearing of the children by air- and bone-conduction was tested at eight pitches (64 to 8,192 c.p.s.)¹ and the results correlated with their medical history, and their proficiency in speech. It is this section which will be treated at greater length in the present paper.

The second part of the work was done in co-operation with Mr. A. G. Wells, the otologist responsible for the children studied in the London schools. It consisted of a controlled experiment to determine what educational benefit could be expected from the use of sound-magnification apparatus for deaf children under school conditions. The desired benefit was, particularly, improvement of the children's own speech, not necessarily their understanding of the speech of others. Anyone who has visited a deaf school will realize that there is room for improvement in the children's speech, particularly in its tone and rhythm, although many of the pupils lip-read with remarkable facility. Since this aspect of the problem is educational rather than medical, this experiment will not here be described in detail. It may, however, be mentioned that from its result we estimated that about three-quarters of the deaf children in the schools would benefit from the use of sound-magnification apparatus.

The occasion of the investigation was an obvious opportunity to compare different testing methods. Therefore although the pure tone audiometer was used throughout, some tests were also done with calibrated tuning-forks, voice, and a gramophone audiometer, and the results of the different methods were compared. Reference to the full report must, however, be made for a discussion of their relative merits.

GENERAL PARTICULARS ABOUT THE DEAF CHILDREN

Among a school population of approximately 500,000 there are about 500 children who are given special educational facilities by the London County Council because of their hearing defect. Every deaf child is considered individually with regard to admission to these schools, and intelligence, and the ability to lip-read, are taken into consideration. But it is a rough rule that if a child can hear a conversational voice 20 ft. away from a teacher he can continue his education in the ordinary school, although his aural condition may require medical attention. If he can hear less than 20 ft. away, but more than 2 ft. away, he is suitable for a school for the partially deaf; and if he cannot hear as far as 2 ft., he should be educated in a school for the deaf.

¹ Cycles per second.

The numbers of children in the different schools which were investigated are shown in Table I.

TABLE I.

Type of school	Number of schools	Number of children tested	Ages years
For the partially deaf ...	5	128	6-13
For the deaf ...	6	199	6-13
For older deaf girls ...	1	54	13-17
For older deaf boys ...	1	75	13-17
	13	456	

The total number tested falls short of the number on the school registers, on account of the exclusion of (1) absentees, (2) infants, and (3) children of very poor mentality who could not understand what was required of them. The 456 children were about 90% of the number on the school lists.

Ages of children at onset of deafness.—The medical record cards of each child were examined to ascertain the cause of the deafness and the age at which it was first noticed. Additional information was often obtained from the written report of the interview between the child's parent and the head teacher when the pupil first attended school. The data thus obtained are only fairly reliable for sundry reasons. The medical examinations were made by several persons and at various times relative to the date of the condition alleged to have caused the deafness. The parents, without intention to mislead, often tended to fix the blame of the child's misfortune on to something definite, such as a minor accident, when the real cause was not obvious. Further, many children were only discovered to be deaf when they had not learned to speak at 2 or 3 years old, and had already had discharging ears, infectious fevers, or undiagnosed illnesses.

TABLE II.—AGES OF CHILDREN AT ONSET OF DEAFNESS.

Age at onset	Percentage of "partially deaf"	Percentage of "deaf"	Percentage of all cases.
Under 2 years	32	75	64
At 2 "	8	3	4
" 3 "	8	4	5
" 4 "	13	4	6
" 5 "	8	4	5
" 6 "	9	3	5
" 7 "	6	2	3
" 8 "	3	1	2
" 9 "	6	1	2
" 10 "	4	1	2
" 11 "	3	1	1
Over 11 "	0	0	0

Those cases in which a record existed concerning the date of onset of the deafness have been summarized in Table II. The striking feature is the early age at which the majority of the cases started, both among the "partially deaf" and the "deaf", especially as most of the errors would tend to make the recorded age later than the true figure. That disease as well as congenital defect shares in this early incidence is shown in Table III in which the figures are taken only from children whose deafness started from otitis media. The relative number of cases of this origin in which the date was uncertain has been included, because in this condition the gradual onset creates a very real difficulty even with careful observers. It will be seen that as many as 53% of the cases of otitis media started during the pre-school period of the child's life.

TABLE III.—AGE OF CHILDREN AT ONSET OF OTITIS MEDIA.

Age at onset	Percentage of 178 cases	Age at onset	Percentage of 178 cases
1 year	16	8 years	1.5
2 years	12	9 "	3.5
3 "	11	10 "	3
4 "	14	14 "	1.5
5 "	10	12 "	0
6 "	8.5	13 "	0
7 "	4.5	Uncertain age	13.5

TABLE IV.—CAUSES OF DEAFNESS.

Cause	Percentage of all cases
Deaf from birth	42.5
Deaf from infection of ears, associated with a specific fever...	18
Deaf from infection of ears, not associated with a specific fever; including cases of ear discharge of uncertain cause	16
Meningitis and brain diseases	6
Congenital syphilis	2.5
Trauma (definite history)	1
Uncertain	11.5

Nearly one-half of the children were said to have been deaf from birth, in spite of the general unwillingness of parents to admit this. About one-third of the total number of cases started with otitis media, and in approximately one-half of these the onset was associated with an acute specific fever. The percentage figure for meningitis and brain diseases is small, but perhaps the most accurate in the table, as the illness with sudden, very severe deafness, after full development of speech, presents such a striking and sad picture that confusion with any other cause of deafness is unlikely. The figure for congenital syphilis on the other hand is probably the least accurate. Not only is a reliable history difficult to obtain, but also children with well-marked stigmata, and even positive Wassermann reactions, may have had discharging ears at some time before the relatively late age at which deafness due to this cause occurs. Trauma was disregarded in the history unless the accident was well authenticated and medical treatment had been obtained at the time. About one-tenth of the histories had to be disregarded, either because the cause was entirely unknown or because the child had suffered from more than one condition, either or both of which might have been the true cause.

The cases of otitis which were associated with a specific fever at the onset are further analysed in Table V. Measles and scarlet fever accounted for more than half these cases.

TABLE V.—SPECIFIC FEVERS CAUSING DEAFNESS.

Specific fever	Percentage of cases of this type
Measles	37
Scarlet fever	22
Diphtheria	12
Whooping-cough	8
Mumps	4
Pneumonia	3
German measles	1
Measles, followed by scarlet fever	2
Measles, followed by scarlet fever and pneumonia	1
Measles, followed by whooping-cough	3
Scarlet fever, followed by diphtheria	2
Scarlet fever, followed by whooping-cough	1
Whooping-cough followed by pneumonia	4

THE HEARING TESTS

It was considered to be more suitable, as well as more practical, to test the children in their own environment rather than in a sound-proof room in a research laboratory. A quiet small room was allocated in each school for the testing. The amount of background noise in the room probably did not exceed 30 db.¹ above the threshold of audibility, and as the maximum amount of hearing of any child in the schools was equivalent to an ability to hear a conversational voice 20 ft. away, which corresponds approximately to 35 db. hearing loss, this arrangement was considered to be satisfactory.

The children's ears were inspected by Mr. A. G. Wells shortly before the date of the hearing test, and arrangements were made, when necessary, that wax or discharge should be removed on the morning of the test day.

The results of the tests might have been unreliable, for several reasons. The child might not have understood what was required of him. He might not easily have been

¹ decibels.

able to judge when the sensation stopped. He might have been bored or tired, or have intentionally deceived. Further, the result obtained might not have been typical of his usual condition, owing to physiological day-to-day variation, or to a temporary respiratory infection. The hearing of children with otitis media is well known to vary greatly from time to time. The last class of inaccuracies would have affected the individual record of the child, but probably not the general conclusions from the determinations, as some of the tests were made in the summer and some in the winter. The greatest total error would probably have occurred among the severely deaf, with whom communication was difficult, and who had little or no experience of hearing. Some idea of the order of accuracy was obtained in a series of re-tests with some of the "deaf" children, when three tests were made at about six-monthly intervals, and the agreement between the results was found to be sufficiently satisfactory.

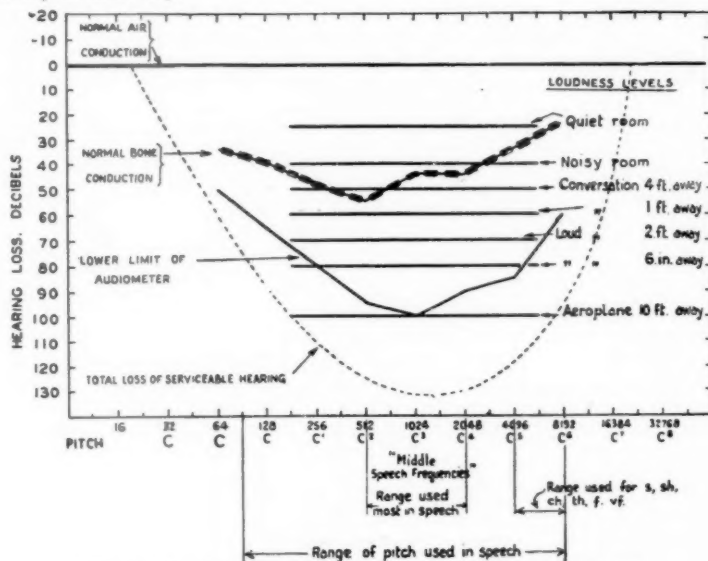


FIG. 1.—Pure tone audiometer test result form with reference lines.¹

Recording of results.—The results of hearing tests at various pitches are more easily described graphically than in words. A blank form such as is commonly used for plotting hearing loss against pitch frequency is shown in Fig. 1, the curve obtained being often called an audiogram. In the same figure the lower limit which could be reached with the audiometer in use has been included and also some reference lines to illustrate in practical terms the range of pitch and of sound intensity. (The lines have been drawn straight for clarity, not because the intensity is really evenly distributed at all pitches within the range.)

MEASUREMENTS OF NORMAL HEARING OF CHILDREN

It was considered advisable to make some measurements on children with normal hearing. The zero line of the pure tone audiometer used in this work is reported to have been made by averaging the results of the minimal audible loudnesses which could be detected by 72 ears of adults in a sound-proof room. There is no indication supplied with the instrument, or in the literature, of the degree of variation among

¹ Figs. 1-16 are reproduced from the Medical Research Council Special Report Series No. 221, by Permission of the Controller of H.M. Stationery Office.

the "normals". The same remark applies to the "normal" bone-conduction line. Further, it is an assumption that lines are the same for children and for adults. The ideal procedure would have been to have re-determined the lines for a large number of children of the same age-grouping as the deaf children. This was not practicable. A good sound-proof room, suitable for such fundamental measurements, was not easily available. Also it would have been difficult to obtain permission for normal

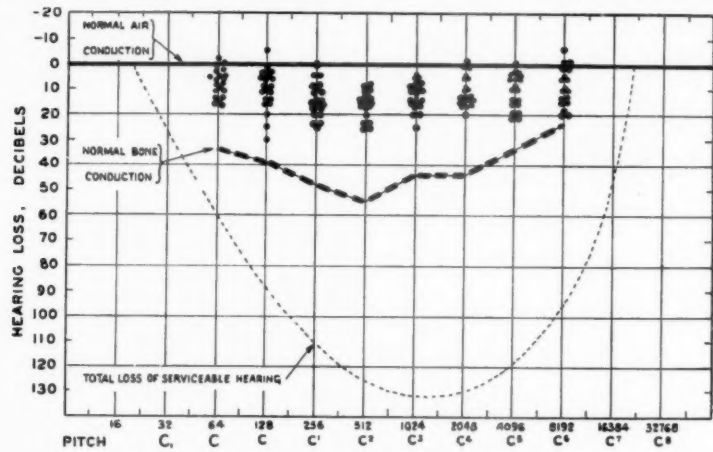


FIG. 2.—Air-conduction of children with normal hearing.

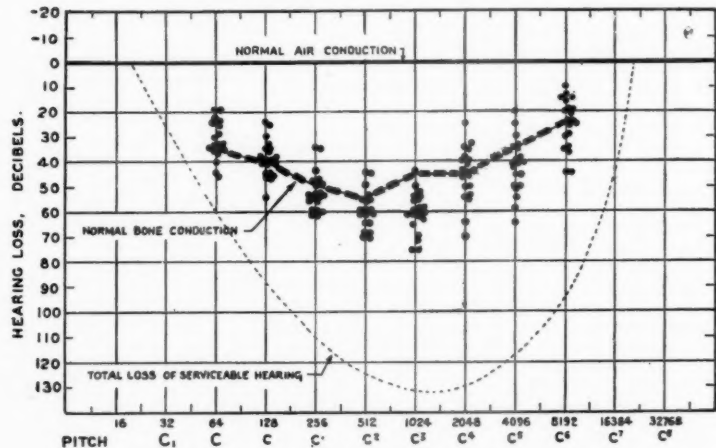


FIG. 3.—Absolute bone-conduction of children with normal hearing.

children to leave school for such a purpose, even if the use of a perfect sound-proof room could have been arranged. It was therefore decided to test a small number of normal children in their school, just like the deaf children, mainly so that a rough idea could be obtained of the range of individual variation.

The tests were made in a spare classroom of an elementary school in central London, which looked out on a quiet blind alley. There was a slight background

of noise from distant classrooms, which was audible to these children, although it would not have been to slightly deaf ones. The school had been visited in the same week by the special nurse who was in charge of the routine hearing testing in the district with the gramophone audiometer. Ten children, between 7 and 13 years old, were chosen who had passed the gramophone audiometer test not more than three days before, who had not a cold, and who were said never to have had running ears.

Air-conduction results with normal children.—Fig. 2 shows the composite audiogram for the air-conducted hearing of the ten children. Each dot denotes a result obtained on one ear. It will be seen that the points form a band about 20 db. wide. The level of the middle of the band is slightly below the zero level, and is farthest (15 db.) from the zero at the middle of the pitch range, which is that region which would be carrying the distant class voice sounds which made up the background noise. Thus it seems probable that there is no appreciable difference between the auditory thresholds of adults and children at the pitches examined, and that the present determinations differed from those indicated by the zero line on account of the influence of the room noise on the ear not under test and the consequent distraction of attention.

Absolute bone-conduction test results on normal children.—Fig. 3 shows the results of the bone-conduction tests, performed with ear-stops¹ in both ears to shut out air-conducted noise. The mean of the points coincides with the line drawn for normal bone-conduction hearing within 5 db., except at 1,024 c.p.s. where it is 15 db. below. The scatter of the points is greater than those of air-conduction tests, and wider for the higher frequencies than for the lower. Between 64 and 512 c.p.s. the determinations lie in a band 25 db. wide, at 1,024 c.p.s., 30 db., and thereafter about 35 or 40 db. wide. The bone-conduction tests were subjectively more difficult than the air-conduction tests. The results give no indication as to whether the increased scatter represent a true increase in individual variation in bone-conducted compared to air-conducted hearing, or whether it was due to increased experimental error, or to both causes. However, it was assumed for the present work that :—

- (1) The normal bone-conduction line represented the mean result of the bone-conduction hearing of children with normal hearing.
- (2) No bone-conducted hearing could be considered abnormal unless it was different by more than 15 db. from the mean figure between the frequencies of 64 and 1,024 c.p.s., and above this frequency 20 db. different.

Relative bone-conduction test results.—On the same occasion as the above tests others were carried out without the use of ear-stops. While not essential to the main purpose the opportunity was taken of demonstrating quantitatively the difference between the relative and absolute bone-conduction tests. The results are represented in fig. 4 in a manner similar to that used for figs. 2 and 3.

It will be seen that the scatter is similar to that of the absolute bone-conduction tests, so that simultaneous air hearing of the room noise did not affect the distribution. It should, however, be emphasized that the room noise was small and approximately uniform in intensity. Under less constant conditions other results might easily have been observed. But the level of the mean of the points is below the normal line and below the mean line of the absolute tests in the middle of the pitch range. In fact the difference between the absolute and relative curves roughly resembles, both in pitch and intensity relationships, the difference between the mean air-conduction determinations on these children and the normal air-conduction line. That this is so is not surprising, as the amount and character of the room noise affects both differences: in the first case through the air-conducted hearing of the room noise with both ears on the bone-conducted hearing of the tones of the audiometer with one ear, in the second case through the distracting effect of the air hearing of room noise with one ear on air-conducted hearing of tones with the other. It appears that the intensities of the two differences are nearly equal in a quiet room.

¹ Luxton type, made of cotton-wool with wax handle, supplied by Messrs. Siebe, Gorman, and Co. Ltd.

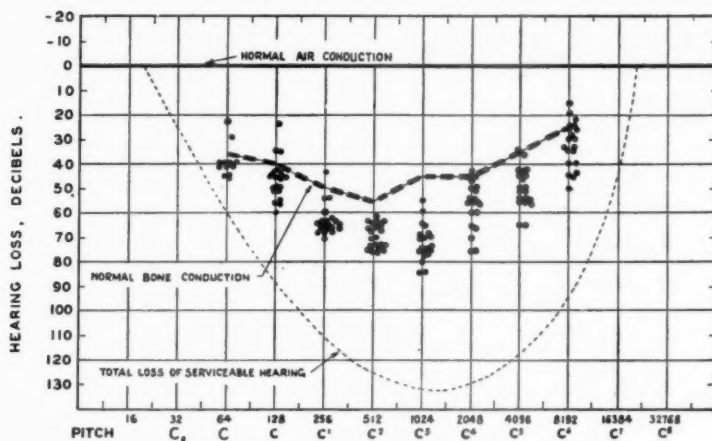


FIG. 4.—Relative bone-conduction of children with normal hearing.

HEARING TEST RESULTS WITH THE DEAF CHILDREN

The shapes of the air-conduction hearing curves.—These curves were fortunately not of infinite variety. They could usually be assigned to one of four general types:—

- (1) Approximately straight lines.
- (2) Curves with a concavity in the middle.
- (3) Curves sloping down from left to right.
- (4) Curves extending over 1 or 2 octaves only.

Such types are illustrated in figs. 5, 6, and 7, and will for convenience be referred to hereafter as:—

- (1) Uniform loss type.
- (2) Middle-tone maximum loss type.
- (3) High-tone maximum loss type.
- (4) Patch type.

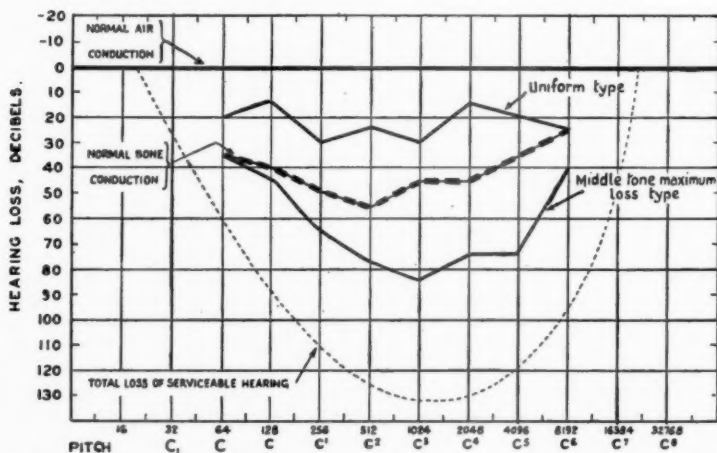


FIG. 5.—Uniform and middle-tone maximum loss types of air-conduction hearing curves.

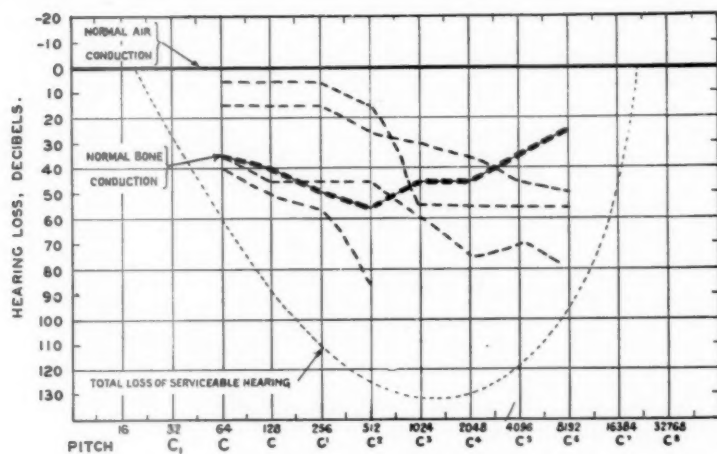


FIG. 6.—Types of high tone maximum loss hearing curves.

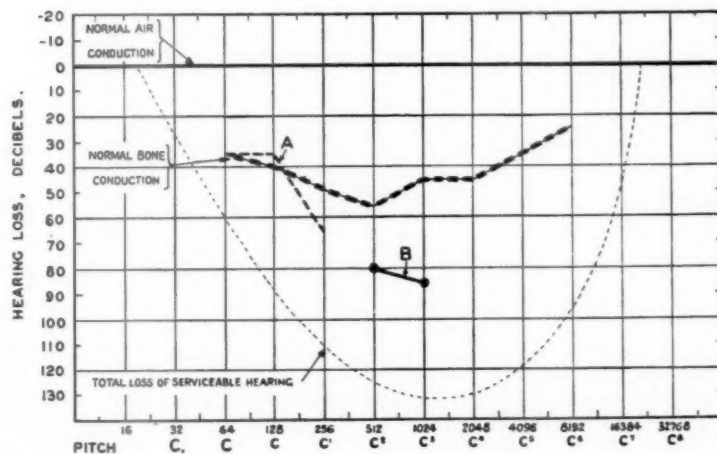


FIG. 7.—Types of patch hearing by air-conduction.

Maximal loss in the low tones occurred in one case only, this uncommon type apparently being even rarer in children than in adults. The uniform loss type was uncommon. The patch type, like that designated "A" in the figure is probably an extreme case of the high-tone maximum loss type, and the distinction between them an arbitrary one. The patch type B, situated in other parts of the pitch range, was less common than type A.

The shapes of the air-conduction hearing curves and the cause of the deafness.—The cause of the deafness was considered in relation to the type of audiogram, in order to

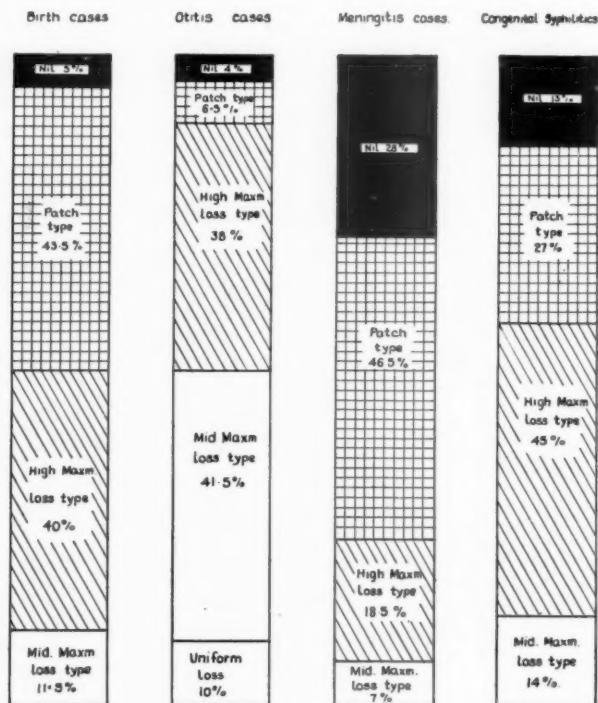


FIG. 8.—Types of air-conduction hearing curve and causes of deafness.

see whether there were such correlations as would allow any estimate of the site of the damage to the ear to be made from a study of the shapes. The four columns in fig. 8 represent the common causes of deafness, and each is subdivided in proportion to the percentage number of ears which were found associated with a particular type of audiogram. The commonest lesion in congenital deaf-mutism is a lesion in the inner ear, although other malformations do occur. Most of the children deaf from birth gave either the high-tone maximum type or had only a patch of hearing. Middle-tone maximum types did occur in this group, but amounted only to 11%. No hearing

at all could be detected in 5% of these cases, and in 3% of all the children in the schools. This figure is very small, but the rarity of complete deafness has been remarked by other workers.

These proportions are strikingly different among the children whose deafness started with otitis media, when high- and middle-tone maximum types occurred in about equal numbers, and uniform loss patches, and cases with no detectable hearing were each small minorities.

It is well known that long-standing or severe otitis media is a common cause of inner ear damage owing to spread of infection. It is tempting from the results obtained to postulate that very slight otitis media causes audiograms of the uniform type, as these always occurred with slight hearing losses and normal bone-conduction: and that a more severe otitis media, when however the infection remains in the middle ear, gives the type of curve with the central depression. No change in the theory of the conducting function of the middle ear is thereby necessitated, as it would be a physical system of incredibly perfect design which would conduct all frequencies equally well, and it is already known that the ear is not acoustically perfect. It is only necessary to suppose that the middle ear is so designed that it normally conducts notes of medium pitch more efficiently than the low or the high, so that when its action is impaired, the middle notes are not carried to the inner ear so well as others. When the infection has spread to the inner ear, high-tone maximum loss, or the patch type of audiogram, or no hearing may result.

In the meningitis group a patch or no hearing was the usual finding, although both the other types of curve were found in small numbers. As meningitis causes damage to the nerves passing through the inflamed membranes of the brain, if all the fibres were affected, total deafness would result; if some remained intact, a patch of hearing would remain. The internal ear may also be affected in meningitis, causing high-tone deafness. So the distribution of curves among most cases due to this cause is easily explained. The small number of middle-tone maximum curves are more difficult to fit in with the pathological condition unless selective nerve-fibre damage is supposed; but these results may perhaps be due to errors in diagnosis or history. The total number of meningitis cases was so small that a single error assumes undue importance.

The congenital syphilis proportions resembled the other congenital cases, but as has already been pointed out, these figures are far less reliable than the others, owing to the small numbers and doubtful histories. The small number of middle-tone maximum curves were probably due to middle-ear disease occurring in congenital syphilis, or to errors in diagnosis.

These findings and suggestions do not conflict in any way with those of the research workers at the Johns Hopkins Hospital, Baltimore, who are examining after death the ears of patients with general diseases whose hearing was tested shortly before death.

SOME SPECIAL CASES OF AUDIOGRAMS OF DEAF CHILDREN

Hearing Curves of Members of the Same Family.

(1) Twins. There were two pairs of deaf twins among the children examined and the audiograms of each pair were very similar. The curves of one pair are shown in fig. 9. The girls were born deaf, and can hardly ever have used their ears during their sixteen years of life.

(2) Three sisters. Fig. 10 shows the audiograms of three sisters who were all more deaf in the high frequencies than elsewhere, although the general level of the curve is different in each case. These curves are typical of many audiograms of families where there were several deaf children. While there is often a general similarity in the slope of the curves, the levels are different. It is not surprising that of the three sisters

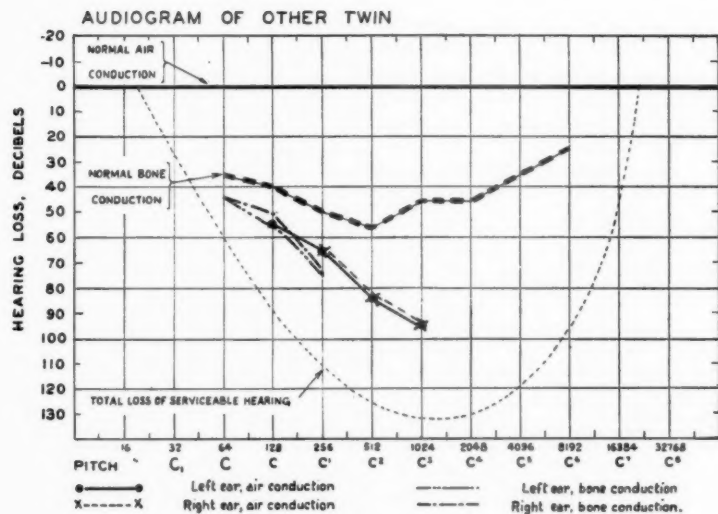
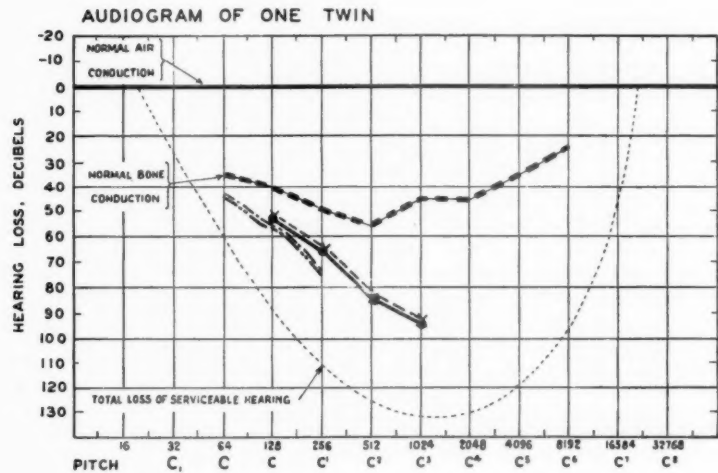


FIG. 9.—Hearing curves of twins.

represented in fig. 10, the speech of the second is the worst, although her intelligence is good, and that the youngest has enough hearing for it to be easily noticed in ordinary life. Her speech was self-taught, but is defective because of the unevenness of her hearing. The other two came to school dumb.

The effect of a respiratory infection on the hearing.—An intelligent girl aged 12, subject to otorrhœa, was tested one week when she had a bad cold, and again a week later when she had recovered. The hearing curves are shown in fig. 11. It will be seen that on the first occasion the air- and bone-conduction curves were almost identical, as if the middle ears were completely out of action. On the second occasion the bone-conduction was the same, but the middle ears had recovered considerably, as shown by much higher air-conduction curves. The change, in terms of the ability to hear the spoken voice, would be (approximately) from a shout in the ear to conversation at 7 ft. This example gives an idea of the difficulty with which these children and their teachers have to contend in school.

Hearing curves of a child said to be aphasic.—No child with normal hearing but without normally developed speech was found among the deaf children, although such

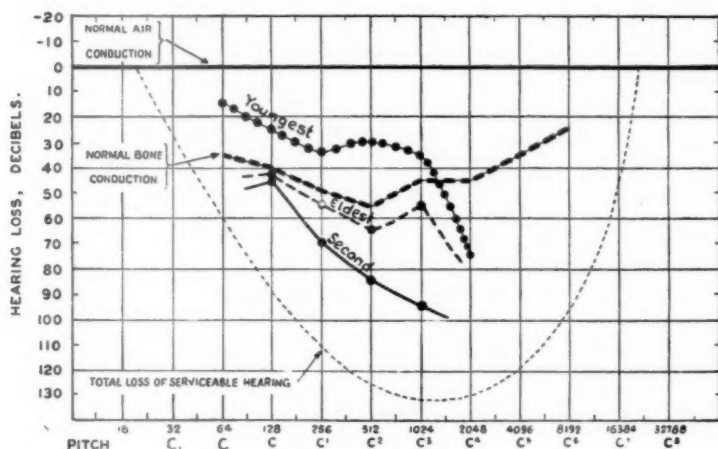


FIG. 10.—Hearing curves of three sisters.

children would have been sent to these schools under existing educational arrangements. True congenital aphasia is, however, known to be rare. But several children who were dumb had been put down on the school records as possibly aphasic, when they had come at a very early age for diagnosis, too young to be tested by any method, but with evidence or history of some hearing. Most of these had later proved to be either cases of high-tone deafness with detectable hearing in the lower pitches, or children who could only hear a few inches away from the ear, and who consequently did not learn speech spontaneously, although even their parents could perceive that they were not totally deaf, and therefore resented the suggestion that they were "deaf and dumb." The confusion between high-tone deafness and aphasia usually occurs when the child can hear the low-pitched sounds of everyday life, but not the high. But mistakes can also happen with cases of deafness maximal in the middle frequencies, as exemplified by fig. 12 (p. 97) which shows the hearing curves of a boy who was said to be aphasic by his teachers, even after several years of school life. The argument used for the diagnosis was that he could pick up tunes from barrel-organs,

but had never spoken properly. It will be seen that he had enough hearing in the right pitch range to enable him to do this. In the absence of scientific data concerning

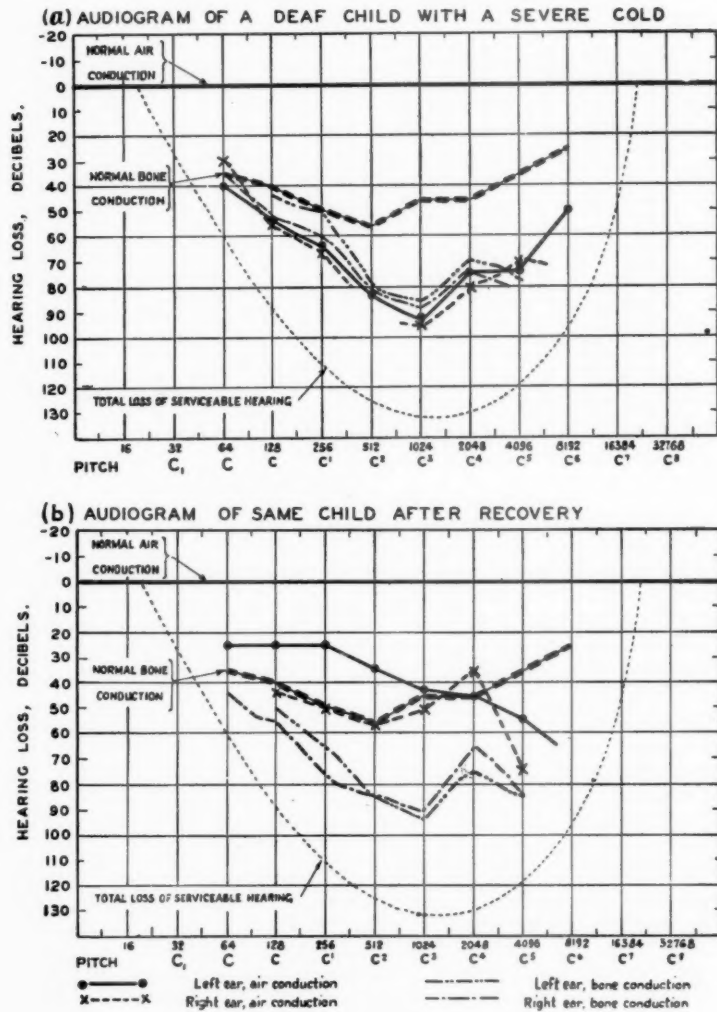


FIG. 11.—Effect of a respiratory infection on the hearing.

barrel-organs, the loudness of radio music has been indicated in the figure, and it will be seen that the amount of his defect was such that he could easily hear it at close

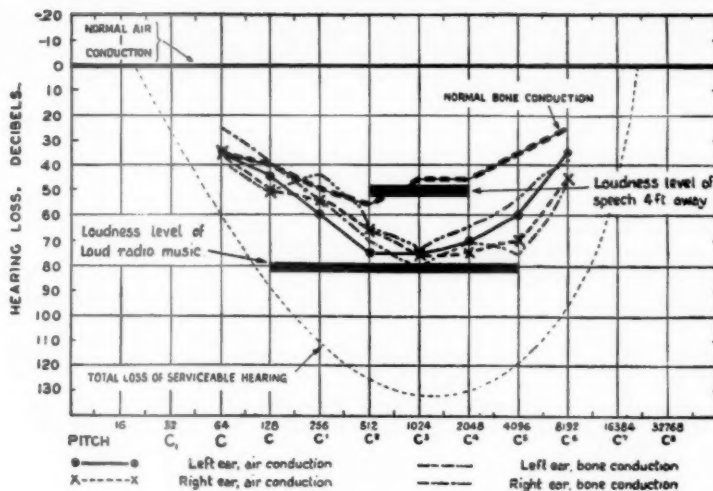


FIG. 12.—Hearing curves of a child said to be aphasic.

range, although he would not hear speech except at about a foot away, and so would not acquire it properly by his own unaided efforts.

PROFICIENCY IN SPEECH

Speech is ordinarily learned by hearing and imitating. What is not heard cannot be copied, hence speech has to be taught by special methods to those who are born severely deaf, or who become so in infancy, the process needing infinite care and patience on the part of both teacher and pupil. Speech is an urgent necessity for the normal psychological development of these children, as well as for their educational and social needs. The final product of the speech of the pupils varies greatly, and depends on many factors. Most of them gain enough ability to be able to express themselves freely to their relatives and friends, although with a somewhat limited vocabulary. Speech of the severely deaf at its best is understandable even to those who are unaccustomed to it, but it is rarely, if ever, normal in sound. There is a peculiarity of timbre about taught "deaf speech" which defies description. The abnormalities are of tone, accent, and rhythm, rather than of articulation. An ability to understand a deaf child's speech readily, and even to ignore its abnormality, is soon acquired if one associates much with the deaf, but the difference from normality is great, and brings a social distinction which is not remedied by the most perfect lip-reading.

Some children come to school dumb although they are not completely deaf to the ordinary voice, because if they can only hear, say, a foot away from them, they do not hear enough of what goes on around them to enable them to acquire speech in infancy in the usual way. But under skilled tuition these children with a little hearing come to speak with a much more natural timbre than those who have never heard the human voice.

The inability to copy that which is not heard applies not only to speech in general but also to speech components. The commonest example of this is heard in the frequent omission of S and Sh from the speech of moderately deaf children with

normally developed powers of conversation, whose deafness is greatest in those high frequencies (about 6,000 c.p.s.) which are essential for the recognition of these components.

If severe deafness occurs suddenly during school life a child may come to speak quite incomprehensibly, if educational care is not taken of the speech normally acquired, but no longer heard.

Hence the speech problems which face the teacher of the deaf are in three different categories: to correct minor defects of the "partially deaf"; to teach speech and vocabulary to the severely deaf; and to preserve the speech and to enlarge the vocabulary of those children who have become suddenly severely deaf after the normal acquisition of speech.

Speech defects among the "partially deaf".—Among the educationally "partially deaf" 66·5% were said by their teachers to have speech which could be considered normal for their age and social class. Defective speech was evident in 33·5% and omission of S and Sh from their words was the commonest fault. Of those children with defects, 60% had maximal hearing loss in the high pitches: 39% in the middle tones, while 1% had defective speech with uniform hearing loss. Hence, although defective speech was most often associated with high-tone deafness, it was not confined to this type.

Speech defects of the "deaf".—In the speech education of these severely deaf children, there are three important considerations which affect the results of the special educational methods. These are:—

- (1) The intelligence of the child.
- (2) The age of onset of the deafness.
- (3) The amount of hearing.

The intelligence of the child naturally affects its ability to profit by the educational methods. The second and third factors determine to what extent the normal method of learning speech can assist the special methods.

During the investigation under discussion, the teachers were asked to report briefly on the speech and the intelligence of each child whose hearing was tested. The general educability of the child for school subjects was taken as an index of intelligence for the present purpose, not an expression of the aptitude for learning speech nor of facility in hand work. Standards regarding speech varied considerably in different schools, but broad divisions were made into four classes:—

(1) Natural quality speech, with or without minor defects	... designated as	N.
(2) Good "deaf speech", age being considered: also natural quality speech with major defects in articulation	... designated as	Gd.
(3) Fair speech for a deaf child of his age	... " "	F
(4) Poor speech for a deaf child of his age	... " "	P.

Speech and age of onset of deafness.—In fig. 13 the children in the schools for the "deaf" have been considered in relation to their proficiency in speech and the age of onset of their deafness. It will be seen that after the age of 8 all the speech was natural or good "deaf speech", but below that age the relative number of pupils with poor or fair speech increased, until of those under two years of age when deafness commenced, nearly 70% are included in these categories.

Speech and intelligence.—The part that intelligence plays is indicated in fig. 14 where the association of intelligence and proficiency in speech is studied among children, all of whom became severely deaf before they were 2. They constitute 64% of the children in the schools, and have been considered in two groups—those in the junior schools and those in the trade schools for older children. This arrangement gives an idea of the effect of length of school life. In the trade schools the pupils spend one-half of each day learning ordinary school subjects, and the other half the special requirements of their trade. The two groups are not strikingly

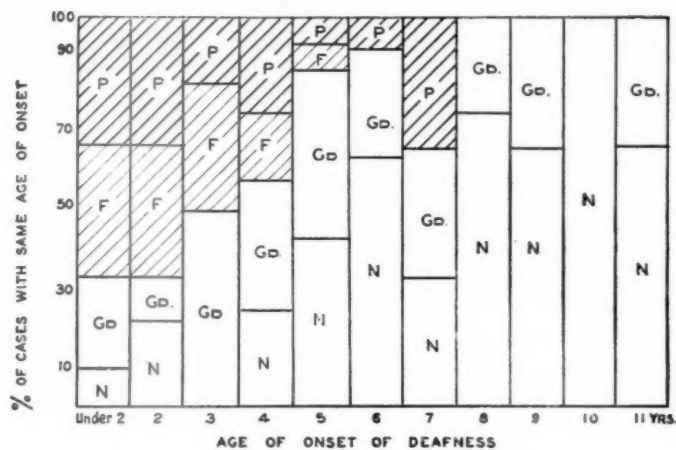


FIG. 13.—Proficiency in speech and age of onset of deafness.

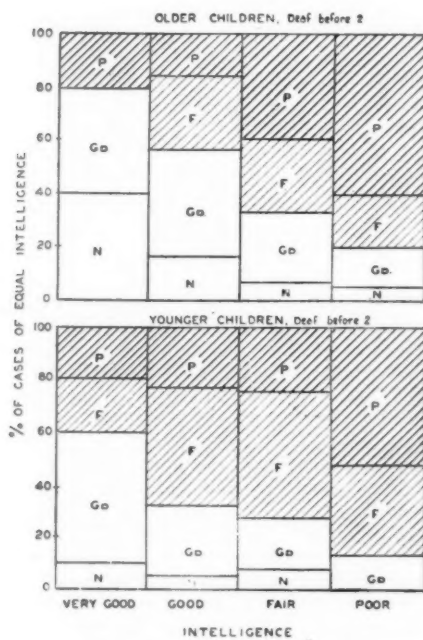


FIG. 14.—Proficiency in speech and intelligence.

different, although the percentage of fair speech is less among the older than the younger. The frequency of inferior speech increases with decrease in mental ability in both cases. In spite of this there were about 20% of children in both age-groups with very good intelligence who had poor speech.

Speech and deafness.—The relation between the proficiency in speech of the children and their amount of hearing loss has been considered. The measurements with the pure tone audiometer for the better ear over the range of frequency used most in speech (512 to 2,048 c.p.s.) have been averaged to obtain a figure representing the loss of hearing for speech. The number of cases having any one degree of hearing loss (within 10 db.) was counted. The children in each hearing deficiency group were then sorted according to their proficiency in speech, and the numbers expressed as percentages of the total number with this amount of hearing defect. The groups

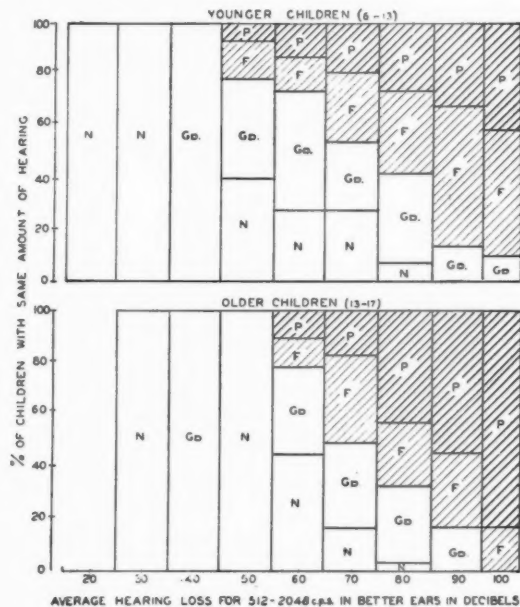


FIG. 15.—Proficiency in speech and amount of hearing.

were subdivided into older and younger children as before, and the results plotted as in fig. 15.

The figure demonstrates well that even small amounts of hearing have a considerable effect on the proficiency in speech. At 30 db. loss, or less, normal natural speech was the rule. Between 30 and 50 db. loss, natural, or good but defective speech was more common than any other, although a few cases of poor or fair speech occurred among the younger children. Thereafter as the hearing loss increased, the percentage of fair or poor speech increased greatly. Among the older children with a hearing loss of over 90 db., the speech of more than 80% was described as poor by their teachers, in spite of many years special tuition, and regardless of their intelligence. None, even of the older children, with this degree of defect had good "deaf speech".

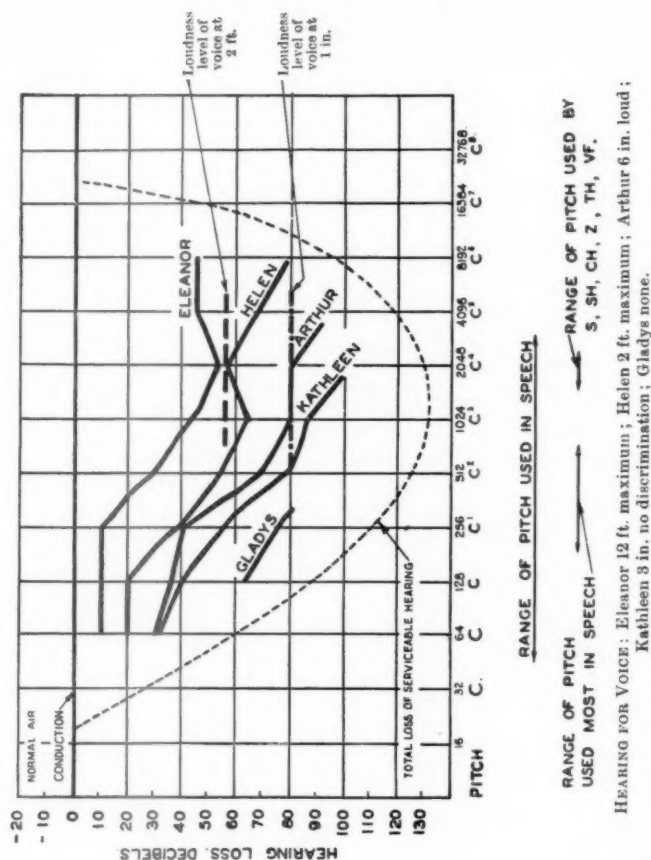


FIG. 16.—Effect of hearing on speech—hearing curves of typical cases.

To exemplify this quantitative relationship between deafness and speech development, five children between 11 and 12 years old were chosen, all of whom were deaf before they were 2, but to different extents, and who had been in a school for the deaf at least four years, and had enough intelligence to be regarded as good pupils. Their audiograms are shown in fig. 16. Arthur, Kathleen, and Gladys were dumb when they came to school.

Eleanor's speech sounds natural, and Helen's is of natural tone and easily intelligible, although the omission of *s* from her words and the confusion of *sh* and *ch* are easily evident. Arthur's speech is intelligible, but slow and obviously defective. Kathleen's speech, which is very good "deaf speech" is intelligible but odd in sound owing to the unnatural timbre and imperfect intonation and phrasing, although there is more phrasing and intonation than usual with "deaf speech." Gladys's speech is largely unintelligible to the unaccustomed, if they have no idea of what she is saying. It should be added in fairness that she would be understood by her teachers and family, although her vocabulary is limited compared with that of hearing children of her age. The speech of these children has been recorded on a gramophone record which unfortunately cannot be reproduced in print.

Physical Aspects of Tinnitus

By C. HAMBLEN-THOMAS, F.R.C.S.

TINNITUS may be described as the response of the auditory part of the 8th nerve and its higher centres to abnormal stimuli. The stimuli may arise external to the organ of Corti, within the organ of Corti, or central to the organ of Corti, and may be physiological or pathological stimuli. The 8th nerve, with the organ of Corti, is comparable to any other sensory nerve of the body, and its end-organ.

Like that common symptom a "headache", tinnitus has many causes, and there is very little accurate information on its essential cause. In describing the physical basis of head-noises, a description also of the physiological and pathological conditions accompanying them is necessary. I do not pretend that what I have to say is anything approaching a complete explanation of the physical causes of tinnitus, but it is a preliminary consideration of the possible physical factors in the causation, from information at present at our disposal. There remains much useful investigation to be done, and whatever may be discovered will be a further step forward in helping patients with this distressful symptom.

I think one may take all tinnitus arising from middle-ear conditions as due to a direct stimulation of the cochlea by sound. But those arising elsewhere may be due to the result of nerve impulse or action current effect.

I have attempted to classify tinnitus as follows: (1) Extrinsic, arising outside the inner ear. (2) Intrinsic, arising within the inner ear, including the 8th nerve and its central tracts.

Extrinsic.

Movements in the middle ear: drum, muscles, moisture.

Muscular movements outside the hearing apparatus.

Cardiac and vascular: arteries, capillaries, veins.

Bony resonance.

Open Eustachian tube.

Intrinsic.

(1) *8th nerve*

Hyperæsthesia of 8th nerve Wever and Bray

Action currents 8th nerve currents

(a) normal; (b) conducted to; (c) injured nerves

(2) *Cochlea.*

Vascular changes Stapes

Pressure on perilymph Round window

Methods of Investigation of Tinnitus.—Estimation of noises heard:—

(1) By observing and recording them by: (a) Otoscope, (b) microphone and amplifier.

(2) By audiometer tests: Hesitation at frequency strength required to drown the tinnitus.

(3) By the study of Wever-Bray effects and action current.

EXTRINSIC TINNITUS

Observed movements in the middle ear synchronous with tinnitus.—Both Politzer and Löwy have reported movements of the tympanic membrane synchronous with the sounds heard in the ear by the patient.

Normal movements of the middle-ear apparatus in response to sound have been recorded with the manometric flame, by reflection from the drum, or by a lever attached to the ossicles. With sound falling on the drum, corresponding vibration movements have been demonstrated; and similarly, various observers have noticed the drum under movement in cases of tinnitus. This type of tinnitus production is

probably due to the same mechanism as in normal hearing. The maximum movement of the drum, observed by microscope, is about 0.4 mm. Again, I have observed a pulsating meniscus of fluid between the edges of drum perforation and the oval window to be associated with a pulsating hum (about 1.028 D.V.) complained of by the patient, and probably produced by means of surface tension variations.

Tinnitus is most accentuated in those chronic ear conditions in which the drum is intact, and the conduction of sound outwards is thus prevented. Again, bone-conduction is also relatively increased in middle-ear disease, since sound from outside the ear is damped, and, for this reason, normal extrinsic sounds arising in the chest, pharynx, mouth, and throat, now become noticeable. For instance, Wever's test is a result of this condition. These sounds would be heard similarly in an absolute silence chamber. As an example of this damping of sound, if the meatus is temporarily plugged, a click produced in the pharynx becomes more audible to the subject.

Bone-conduction is undoubtedly a greater factor in adults than in children, because of the greater density of their bone, for the reason that conduction of sound increases with the density of the conducting medium; it is no doubt partly for this reason that tinnitus is uncommon in children. It is also said that endolymph pressure in children is also more stable; we know that headaches are uncommon in children—possibly for the same reason.

Fabricius and Schaefer attribute some head noises to frictional sounds of the small bones: this is possibly due to rapid apposition-and-relaxation percussion movements of the incudomalleal joint, caused by spasmodic contractions of the stapedius muscle. (Hartridge assigns this movement to the stapedius.) This can be up to 230 movements of the muscle per second, and a high-rate tapping noise would result. There is also the possibility of frictional noises in the joints, due to osteo-arthritic or rheumatoid changes. Many patients suffering from rheumatism have head noises, and there is no reason to suppose that some of them have not affection of the small ossicle joints.

Noises of Muscular Origin

Pharyngeal muscle movements.—Politzer was one of the first observers to record noises due to palatal and pharyngeal muscle movements. The muscle movements cause apposition and separation of the moist Eustachian walls, and this produces a clicking noise that can easily be heard by an observer with the otoscope, and, occasionally, even at some distance from the ear. The sounds are often of a frequency of as high as 70 per second. Again, some are actual muscle contraction sounds with, possibly, overflow action of the tensor tympani, too.

Tinnitus of muscular origin is usually of low frequency, and is described as murmuring, vibrating, and fluttering (frequency 20 to 30 per second).

Masticatory muscles.—Leiri says that the high-frequency noise (a hiss) in the ear, on contraction of the masticatory muscles in a backward direction, is due to the shocks produced by the inferior maxillary muscle and conducted to the cochlea, where waves peculiar to the resonance of the inner ear (which, he says, are about C5) are produced. But Bárány says this noise is due to the contraction of the stapedius.

Tinnitus due to:—

Muscles of the middle ear.—Contractions of the tensor tympani and stapedius. Normally these are at rest, and not contracting.

From contractions of the muscles of the middle ear there may be two factors causing tinnitus: either

- (1) Alteration of intralabyrinthine pressure, with deformation of the organ of Corti and abnormal response to the normal body sounds, so that they become consciously audible as a tinnitus, and thus, an imitation of normal external sound response; or

- (2) The contractions of the muscles themselves may be heard.

These contractions of the tensor tympani and stapedius are produced either by overflow impulses from the muscles of the same nerve supply or by deformity of the muscles themselves, due to middle-ear disease, causing stretching, adhesions to, or fibrosis in the muscles, or altered blood supply, or irritation of the nerve. The tone of a muscle is increased by disease, and so abnormal sounds are produced. Tonic contractions never discharge more than 25 per second. Voluntary contractions are 3 to 50 per second. Adrian has shown, however, that as many as 230 contractions per second can be obtained in a muscle by stimulation. One possible function of the inner-ear muscles is to aid in the production of overtones by the vibrating elements of the middle ear.

The action of the tensor tympani is to draw in the malleus and compress the oval window, so giving a better response to high frequencies. The stapedius is antagonistic to the tensor tympani.

If muscle contractions are weak, the movements are slow, but they rise in rapidity as the contractions increase in strength. Adrian, by actual sound-production with a loud-speaker, has recorded the rise in the frequencies of the nerve muscle action currents up to 200 per second—what one might call "the moan of the muscle". One must consider that the contractions of one of these intrinsic muscles may, in themselves, produce noises of probably a low frequency. This, of course, does not include the effects of the stapes being pressed into the oval window. Cases of 7th nerve paralysis, with consequent paralysis of the stapedius muscle and accompanying tinnitus have been recorded which is possibly due to an altered response by the cochlea to normal frequencies.

In stapedia paralysis the tinnitus may be due to unopposed action of the tensor tympani pressing the stapes into the oval window. Where paralytic contraction has set in, the cutting of the tensor tympani and stapedius has relieved the tinnitus.

But further and more exact analysis of the method of causation of tinnitus in the middle ear is required. There must be further study of the variations in pressure exerted by the tensor tympani and the stapedius muscles on the round window and of their effects on cochlear response. There must be investigation of any noise they may produce in themselves, in contracting. Investigation of electrical variations, however minute, is also required. We know that the maximum movement of the drum, as measured by the microscope, is 0.4 mm.

Middle-ear noises generally are low-toned and intermittent, and most observers are of the opinion that resonance of the middle and outer ear plays no part in head noises, but Kiesselbach says that resonance does play a part, if there is hyperæsthesia of the 8th nerve.

Vascular Sounds

Those of the heart consist of greatly varying frequencies, the first sound being composed of frequencies 13 to 1,000 per second, but the majority are between 30 to 45 per second.

Normal vascular sounds exist, but they are unheard except in a silent room or in conditions where the conductive apparatus is defective and the normal masking by outside sounds is absent.

Auto-auscultation of vascular sounds is a rhythmic effect only when these are of arterial origin. Capillary and venous sounds are relatively continuous. Vascular sounds are strong and hissing, or humming and roaring, and often present a periodicity independent of the pulse rhythm. Tsukamoto and Shinomiya have made some interesting experiments in this respect. There may be no apparent impairment in hearing, but Rinne is usually found to be negative when tinnitus of vascular origin is complained of.

Sounds of the large head arteries.—The principal vessels in the head concerned in tinnitus are :—

- (1) The large head arteries, the internal carotid, and the vertebral.
- (2) The large veins.

But sounds are also conducted up from the large vessels of the thorax and neck to the cranial vessels, especially if there is an abnormality in the former. Plaques and aneurysms are particular causes, and the noise may be a blowing sound or a hum. Occasionally the internal carotid is unusually close to the hearing apparatus. High blood-pressure makes the sounds in the arteries more marked, and generally raises their pitch. These noises are usually controlled by compression on the carotids. Raynaud-like spasm of the smaller arteries is found to occur in certain cases of tinnitus.

With reference to vascular sounds, I have carried out interesting experiments with rubber tubing and the Galton whistle enclosed in the column of water.

Venous sounds.—The vessels principally concerned are :—

- (1) The lateral sinus. (2) The jugular bulb.

The lateral sinus frequently varies in size on the two sides of the skull. Sometimes, also, the lateral sinus is far forward and, more rarely, there is a dehiscence in the bony floor of the tympanum through which the bulb appears. The relation of its pulsations to the tinnitus has thus been able to be observed. The formation of whirlpools in the bulb are given as a cause of tinnitus. I was unable, however, to produce any venous hum in an artificial jugular bulb, but mechanical reproductions often fail where the genuine article succeeds.

Vascular noises are generally increased by closing the meatus, and are more marked where the drum is intact, and also when the bone-conduction is relatively increased.

The venous noise may be a hum or a bellows-sound. It can sometimes be heard through the otoscope as a note with a frequency of C 128 T F. Or it may be heard as a whining sound or a rhythmic hum. The sounds are still heard by the patient when they have ceased for the observer. This variation in vessel sounds depends on slight alterations in pressure or in vessel tone, or in the position of the neck.

Iglauer has shown that venous noises are influenced by rotation of the head and by light pressure on the jugular vein. Rotation of the head away from the ear in which the tinnitus is present increases the noise : this is due to the sternomastoid of the affected side being rendered tense, and so holding the jugular open. In support of this explanation, increased pulsation of the lateral sinus and jugular bulb have been observed when the head is turned away from that side. I have found that pressure on the neck alters the pitch of the noises.

It is difficult to imagine sounds in the smallest arteries and capillaries being conveyed via the conduction apparatus, but they may affect the perceptive apparatus. I shall refer to this latter when I come to an account of the inner ear.

Eustachian Tube

The open Eustachian tube will allow the easy entry of pharyngeal and laryngeal sounds to the middle ear, but it is very doubtful whether the Eustachian tube itself under any condition acts as a resonator.

INTRINSIC TINNITUS

I would like now to describe changes produced in the inner ear as another cause of tinnitus. Vascular changes have already been mentioned as affecting the cochlea or the 8th nerve.

There is a possibility that the internal auditory artery may convey abnormal vascular sounds to the inner ear, and the disappearance of tinnitus when the head is turned has been put down to alteration in pressure of the vertebral artery concerned. But the tinnitus is more often due to the action of the vessel on the perceptive mechanism itself, causing a state of congestion or anæmia.

Persistence of the arterial supply has been shown to be necessary for the main-

tenance of the potential currents associated with hearing described by Wever and Bray, and therefore we may suppose that variations in it will produce alteration in the cochlear reactions, and so tinnitus.

Vasomotor changes enhance irritability of the 8th nerve and cause increased sensitiveness to normal body sounds not otherwise heard.

Diminution of blood supply by spasm of sympathetic nerve origin produces sensory disturbances and noises. Abdominal conditions produce reflex sympathetic effects.

In otosclerosis (osteoporosis) involving the capsule, the tinnitus is probably of vascular origin, and it is enhanced by the fixation of the stapes in the oval window increasing the apparent bone-conduction and limiting the reception of high tones. But it may be found that there is an action current effect, too.

Vasomotor dilatation of ear vessels gives rise to new sound reactions to which the auditory nerve is unaccustomed, and tinnitus is heard as chattering, chirping, and tree-rustling.

Increase of blood-pressure increases the irritability of the 8th nerve, and increases and alters its sensitivity and conduction. Vasomotor and allergic action on the vessels of the ear produces ringing and rushing sounds. These are relieved by curing the underlying condition.

Apoplexy of the ear causes intense tinnitus of sudden onset. Manasse has shown hyperæmia and hæmorrhage into the 8th nerve and spiral ligament to be associated with cases of tinnitus.

Many cases of essentially intrinsic tinnitus, apparently due to arterial conditions, may be the result of the ultimate effect of the blood supply on the 8th nerve or on the cochlea itself.

The 8th nerve.—Two types of current have been shown by Davis to occur in the 8th nerve: (1) Cochlear response, described by Wever and Bray, Hallpike, &c., and (2) true nerve action currents.

A characteristic of most tinnitus is its persistence, with no evidence of fatigue, and this is also a characteristic of nerve-fibre, and, incidentally, of the Wever and Bray action currents found in the cochlea. Synapses may become fatigued, but not nerve-fibres. If the tinnitus was of the character of normal hearing one would expect fatigue—and perhaps, in view of its persistence and long duration, anatomically corresponding degeneration of the cochlea, as happens in the guinea-pig after long stimulation with a single note. There is a probability that some cases of tinnitus are of the nature of a neuritis and that resultant injury currents are set up. These injury currents may be of a frequency of 100 to 400. Again, the damaged fibres may be more susceptible to action currents arising elsewhere in the neighbourhood. For instance, Howe reports a case of a cat with a degenerated left organ of Corti, in which it was possible to pick up a frequency of 500 from the left ear, due to crossed bone-conduction from the good right ear.

Kupfer goes so far as to say that all ear noises are due to nerve currents, but he is probably overstating the facts.

1,000 per second frequency seems to be the maximum that a nerve-fibre can discharge, owing to the length of the latent period; but, as an explanation for the higher frequencies necessary for normal hearing, other fibres may send added impulses, and staggered impulse effects may be produced in the nerve responsible.

The normal inhibiting state of the 8th nerve, in which it does not respond to small, subliminal normal impulses, breaks down in disease or intoxication, and the nerve becomes hyperæsthetic, thus receiving impulses which would not normally affect the hearing. That is, a sub-threshold stimulus now becomes effective.

Local vasomotor changes, and changes caused by inflammation, increase the irritability of the nerve. Slight, prolonged pressure may exalt the excitability, as also a pH increase in the blood, and any increase in osmotic pressure. When in this state, the 8th nerve may become more susceptible to other intracranial action currents.

For instance, the cerebellum discharges nerve impulses of 150 to 250 per second. Adrian has recorded nerve-injury currents of high frequency (150-500-800) on the loud-speaker, characterized by sounds varying from a low note to a high-pitched wail—the nerves, as it were, crying out in pain. Also definite musical notes given by rhythmic discharges with frequencies of 150 to 600 per second are produced as various nerve-fibres take part in the discharge. The nerve discharges have been shown to change from a confused noise into a definite musical note of considerable volume, and this is frequently the description of their head noises given by patients. Adrian thinks these impulses are associated with sensations of the character of pain, and in some patients it is a fact that the noises *are* associated with pain in the ear. Possibly there are in the 8th nerve, fibres of the same character as the pain fibres of an ordinary sensory nerve: we know that a note of great intensity causes discomfort. We must not forget that the 8th is only a specialized sensory nerve, and painful stimuli are possibly recorded as tinnitus.

Higher frequencies than 1,000 per second can be explained by the sending of staggered impulses of ordered sequence over bundles of nerve-fibres situated close together.

A study of the Wever and Bray phenomenon as a possible factor in tinnitus is interesting, since changes in the cochlea which stimulate without destroying it may set up these currents. The Wever and Bray response is not diminished by long-continued stimulation, and we must remember that this is an interesting characteristic of tinnitus, too.

Various alterations in the pressure of the perilymph, due to pressure at the oval window, or vascular changes within the inner ear, leading to increased fluid pressure (cf. glaucoma of the eye) or oedema of the Deiters's cells, may abnormally stimulate the organ of Corti. The Wever and Bray phenomena are intensified by fixation of the round window (Hughson and Crowe) and by increased intralabyrinthine pressure, and they are diminished by limiting the blood supply through pressure on the carotids. The Wever and Bray action currents persist even after destruction of the 8th nerve, but they disappear if the cochlea is destroyed.

Cocaine at the round window suppresses Wever and Bray phenomena: I have found this happen similarly to the noises in two cases of tinnitus in which there was a perforation, and I was able to approach the round window.

Alteration of intralabyrinthine pressure may upset natural and accustomed basilar response, so that normal body sounds stimulate unaccustomed portions of the organ of Corti.

Some head noises of long standing are said to become cerebral in origin. This may be due to persistence of action currents in the auditory tracts concerned.

ESTIMATION OF HEAD NOISES

There is much that may be done in the investigation of tinnitus. In some cases the noises may be heard by the observer through the otoscope, or, rarely, the movements of the contents of the middle ear have been reported in association with them.

So far, a suitable microphone and valve-amplifier have not been produced so that the sounds can be recorded graphically, but it is hoped that a suitable microphone—which is the main difficulty—will be available soon. One of the present difficulties with a sensitive microphone is the exclusion of extraneous sounds.

In the case of many patients it is possible to match their particular tinnitus on the audiometer, piano, or tuning fork. It is interesting to note that, in testing patients with tinnitus, they show a hesitancy in responding to the audiometer at the particular frequency of their tinnitus. Again, the intensity of their tinnitus can be estimated by the amount of sound above normal at the particular frequency which is required to drown it.

I am hoping that, in some cases of tinnitus, I may be able to pick up the action

currents from the round window, as in the Wever and Bray phenomena, and record them: I am hopeful that such do exist in these cases.

Until we can obtain more information about tinnitus we cannot hope to get far in its treatment. It is a very real discomfort to those who suffer from it, and whatever can be done towards relieving them is well worth while.

Discussion.—Mr. E. D. D. DAVIS said that Mr. Hamblen-Thomas had tackled a very difficult subject, about which little was known from the anatomical and pathological points of view. The cases were divided into two classes; (1) those due to local causes, such as otosclerosis, secondary sclerosis, &c., and nothing seemed to cure them; (2), the large majority, in which was a complex mental process. Like vertigo, there were other conditions which caused it, apart from the ear. He was referring especially to psychological conditions. The late Mr. Richard Lake destroyed the labyrinth in cases of tinnitus, but with no beneficial result, and he (the speaker) had himself done a similar operation twice, with no effect on the tinnitus. The late Sir Charles Ballance divided the auditory nerve, but the tinnitus remained unaltered. Tinnitus patients were very sensitive to the caloric labyrinth test, and the reaction was severe, often followed by sickness.

At one time surgeons ligatured the internal carotid artery in an attempt to cure tinnitus, but without much effect. Sir James Dundas-Grant had said that tinnitus was arrested by compressing the carotid artery, but that was true in only a few cases. The effect of muscular action was difficult to assess, but occasionally one saw a clonic contraction of the pharyngeal muscles, which caused a "click" in the ear which was audible to the examiner with an otoscope.

Mr. WATKYN-THOMAS said that one of his difficulties in regard to the treatment of tinnitus was this: As far as he could see to date, the only drugs which had any effect in the treatment of this condition were those which stimulated the sympathetic or raised the blood-pressure. It was agreed that the treatment of tinnitus by sedatives left the patient, usually, in a worse state than before treatment. On the other hand, the only surgical treatment, apart from draining a septic focus, seemed to be destruction of the sympathetic by stellate ganglionectomy. He had never himself done that operation, but several cases had been recorded in which it had been a success. He found it difficult to reconcile those two propositions. Division of the stapedius had been mentioned, but he would give a caution against doing that; he had seen a case in which a colleague had successfully divided the stapedius—a masterpiece of surgical handiwork—and the result was that the patient got a most intractable vertigo, probably from wobbling of the loose stapes in the oval window. It became necessary to destroy the labyrinth. There was no relief of the tinnitus. In many cases where he had done labyrinthotomy for suppuration or for vertigo, the vertigo had ceased entirely, but tinnitus had persisted.

Dr. MYGIND said that by manipulations of the intralabyrinthine pressure, decreasing or increasing it by dehydration or by water tests, an influence on the tinnitus was observed in many cases. In some cases in which dehydration was carried out and the hearing was improved, the tinnitus might temporarily be paradoxically increased. But only some of the tinnitus cases belonged to this group. In some cases he had produced benefit to the hearing and the tinnitus by the treatment he had just described.

Mr. THACKER NEVILLE, referring to attempts to stop the tinnitus by pressing on the carotid, said that he had tried it in one case and the patient had become unconscious. Mr. Davis had said that it was of no use to destroy the labyrinth for tinnitus. He (the speaker) had had a patient—a porter—who said he would commit suicide because of his tinnitus. He (the speaker) had destroyed the labyrinth, and at the same time he destroyed the facial nerve. The tinnitus was cured. In one case tinnitus had been cured by removing the lining membrane of the antrum.

Mr. HAMBLÉN-THOMAS (in reply) said it was necessary to choose carefully those cases in which one compressed the carotid. He did not say that a cure would be obtained in all cases by this means. With regard to hearing a noise when the 8th nerve was cut, he had in mind the possibility of action currents continuing in damaged nerves, or that the memory of the noise might still persist.

The Present Position of the Surgical Treatment of Otosclerosis

By MAURICE SOURDILLE

Professeur à l'École de Médecine de Nantes.

SURGICAL treatment of otosclerosis has become a capital question during the last ten years and cannot be thoroughly dealt with in a few minutes. I will therefore only consider the most important points.

Two kinds of operative procedures are actually used for otosclerosis: (a) Those based on the supposed pathogenesis of the disease (Wittmaack-Heyninx-Rollin and Alonso-Chiarino). (b) Those based on the acoustic results of the labyrinthine "fenestration". (Holmgren's third method and Sourdille's "tympano-labyrinthopexie".)

(a) PROCEDURES DEPENDING ON PATHOGENESIS

(1) Wittmaack-Heyninx-Rollin's method: This was devised by Professor Wittmaack in 1918, and performed on the cadaver by Professor Heyninx in 1925. It has been carried out on patients, by Heinz Rollin at Hamburg, 34 times since 1934. It is called "soulèvement de la dure-mère supra-tympanique" (raising up of the supra-tympanic dura mater). Its technique is endocranial, and consists in separating the dura mater from the antero-superior surface of the petrous bone, and thus lacerating the blood-vessels. As a consequence there is a decrease of the perilabyrinthine circulation and the blood stagnation, which is generally considered to be the first anatomical lesion of the disease. This procedure has no direct action on the actual lesions; its purpose is to stop the progress of the deafness. Some cases have been improved; tinnitus especially has been decreased or suppressed. As, however, the area that has been artificially deprived of blood does not extend beyond the antero-superior wall, it may be feared that the results will be neither complete nor permanent.

(2) Alonso-Chiarino's treatment is quite new, having been carried out only seven times. It is based on the hypothesis that otosclerosis is due to a parathyroid trouble. (dysparathyroidism). The left parathyroid is removed, or some of the thyroid arteries are ligatured in order to decrease the glandular secretion. The cases are as yet too few and too recent to warrant a decision as to the value of this treatment.

(b) PROCEDURES BASED ON THE ACOUSTIC RESULTS OF LABYRINTHIC "FENESTRATION"

History.—The experimental fact that hearing is much increased after the opening of a semicircular canal has been at the origin of a great number of surgical treatments for otosclerosis. Bárány's first and second methods, Jenkins' operation, and Holmgren's first and second methods were unable to maintain the increase of hearing which occurred after the opening of the canal was made, and were consequently given up.

In 1929 Sourdille reported that the benefit to the hearing might be made permanent if a new tympanic system, which would carry vibration to the labyrinth, was combined with the opening of the semicircular canal. He gave his technique the name of "tympano-labyrinthopexy", and has steadily improved it in the last eight years; 140 ears have been, or are being, treated, and a total of 380 operations have been performed.

In 1936 Holmgren described a clever modification of his first technique through

the mastoid, and employed this in 13 cases. He lays open the semicircular canals and closes them with a gold leaf kept in place by a graft of adipose tissue.

Operative techniques.—Sourdille's procedure or "tympano-labyrinthopexy" is completed in three stages: The first, on the external ear, the second on the middle ear, and the third on the labyrinth. An interval of four or five months elapses between each stage.

Stage I: The cutting of and removal of a large area of skin from the outer two-thirds of the postero-superior wall of the external auditory meatus; the healing will take place under a thin, but strong, epithelialized, hairless and glandless tissue.

Stage II: The mastoid cells are laid open, the aditus is exposed, and the head of the malleus is removed, care being taken not to dislocate the incus, which must remain in a high position. The cicatricial tissue obtained in this stage—called "*plastique interne*"—will be used to cover the incus and closes the aditus up to the external semicircular canal. The post-operative treatment will aim at epithelialization, as after a radical mastoid operation. The result is a large pre-tympano-labyrinthine vestibule made of the external auditory meatus *plus* the mastoid diverticulum; this large vestibule is in direct communication with the outside; this is an exo-mastoid operation.

Stage III: The opening of the bony wall of the horizontal semicircular canal, with great care so as not to hurt the very delicate membranous canal. The "*plastique interne*" is applied to cover the opening; it must be considered as an extension of the tympanic membrane, as a new sound-amplifier.

Holmgren's operation is performed in one stage and consists in opening the mastoid process, the antrum, and the external, and posterior and anterior (if possible) semicircular canals. A small piece of gold leaf is applied over each of those labyrinthine openings and kept in place by a graft of adipose tissue filling the mastoid. The wound is closed by sutures and a drainage inserted. The whole procedure takes place inside the mastoid, i.e. it is an endo-mastoid operation.

MECHANISMS OF THE TWO PROCEDURES

Recovery of the hearing is obtained from the opening of the labyrinth, and from this point of view both procedures work in the same way. After the bone is opened, liquid will flow through and the labyrinth will partially empty itself. The vibrations, passing directly through the labyrinthine opening, and also by bone-conduction, will be transmitted to the perilymph; wave movements of the endolymph will ensue and the sound will be perceived.

Maintenance of the recovered hearing will be obtained if the labyrinthine liquids keep their mobility under the action of the vibrations.

(1) In Sourdille's method the movements of the endolabyrinthine liquids result from the transmission of the vibrations by the new tympanic system applied to the labyrinthine opening; the mechanism is analogous to the normal physiological process. When the new tympanic system is once formed, it has no tendency to change, and its function can keep on, so long as the covering of the labyrinthine opening remains soft and elastic. If it happens to ossify, hearing will disappear but, in a secondary operation, the newly formed bone may be taken off; hearing then comes back at once and persists without further modification; local osteogenesis seems exhausted and will not form any new bone again; cases which were operated on eight years ago confirm this opinion.

(2) In Holmgren's operation there are two explanations of the movements of the endolabyrinthine liquids:—

(a) The perilymphatic space remains always half-full of liquid. As the perilymph forms rapidly, Holmgren releases a constant issue of the liquid through the fistula;

if a soft tissue graft happens to adhere to its edges, the labyrinth might get filled and hearing disappear; the application of gold leaf over the fistula obviates this danger. This first explanation is based on the principle of "the half-filled bottle".

(b) A second explanation may be given as follows: If a comparatively heavy foreign body, for instance a small ball of gutta-percha, applied to the labyrinthine fistula, rests closely on the bony wall of the mastoid, so long as it keeps in that position it receives vibrations through the skull and conveys them to the labyrinthine wall and perilymph. It works as a ball inside a small bell—it is the "mechanism of the grelot".

COMPARISON BETWEEN THE TWO PROCEDURES

(1) Holmgren approaches the problem and works out his method from the surgical point of view. His purpose is, by an endo-mastoid operation, to avoid infection and pus formation. The physiological side of the problem is of secondary importance, and the resulting mechanism of transmission appears to be entirely different from the normal one. Further, foreign bodies, such as gold leaf or gutta-percha, may eventually not be well tolerated.

(2) Sourdille works from the physio-acoustic side of the question. His procedure keeps the labyrinthine hydrostatics normal and the vibrations of labyrinthine liquids natural. The question of surgery is second to the due regard for physiological functions. He takes the risk of a mastoid infection, but at a stage when the labyrinth is not yet open and consequently runs no danger; moreover, this mastoid infection can always be brought under control—it is a matter of operative technique combined with protein-therapy.

The long duration of the treatment is largely compensated by: (a) The simplicity of each operative step; each stage has certain definite objects and reaches them easily and successively. (b) Perfect safety, as the three successive stages are managed by open operations followed by careful drainage. (c) Greater local security, as only one semicircular canal is laid open (this step is of course the most delicate for the surgeon and the most dangerous as regards the hearing). (d) An easy second operation if, as is still often the case, the labyrinthine fistula, closed by bone formation, has to be opened again.

INDICATIONS

For the time being one must operate only in cases of primary otosclerosis accompanied by ankylosis of the stapes—i.e. the tympano-labyrinthine form, with negative Rinne and prolonged Schwabach. Operation must not be performed in cases of secondary otosclerosis with even slight inflammation in the tympanum, as in these cases there is a great risk of consecutive necrosis of the incus, and labyrinthine infection.

One must not wait too long before proposing the treatment. The hearing is, as a rule, definitely improved by operation, and from 10 to 20 times more powerful than before.

If the operation is performed at an early stage—say when low voice can still be heard at one metre—a restitution to normal may be expected. But most of the patients refuse the operation at that stage, and accept it only much later when their hearing is more severely impaired; if a loud voice cannot be heard beyond half a metre, results will not be so good, but the patient will be able, with some aid, to resume his ordinary life.

X-ray pictures, and particularly a stereoscopic view of the mastoid, are most necessary in order to determine whether operation is feasible. A very dense mastoid is a contra-indication; access to the antrum may be impossible if the lateral sinus comes too much forward; temporal bone pneumatosis extending forward beyond the site of the temporo-maxillary point is another contra-indication; laying open the

zygomatic cells is a very difficult work and is often followed by infection, pus formation, and necrosis of the incus.

CONCLUSIONS

Faced with a case of otosclerosis, we are now fully aware of the physio-acoustic conditions which allow of the attempt to recover some hearing and to retain the improvement. We are aware also of the surgical conditions which are needed for their realization.

The way to prevent subsequent closing of the labyrinthine opening by bony processes is now the great question to work on; but a gap in technique should not prevent us from carrying on the surgical procedure; in eye surgery, cataracts were removed long before intracapsular extraction was known.

The most general, and apparently severe, criticism against surgical treatment may probably be expressed as follows: How are these modern sanguinary procedures to be reconciled with the old pathological and therapeutical theories of otosclerosis—with the *noli me tangere* of the classics? I do not hesitate to answer that, on account of the positive and successful results at which we have arrived, those old theories should be reconsidered.

Fifty years ago, Politzer expressed the opinion that bony lesions of the labyrinthine capsule were the substratum, if not the causation, of auditory troubles. Since Bárány's report in 1910, surgery has taught us that the pathology and therapeutics of otosclerosis depend chiefly on labyrinthine hydrostatics. I am pleased to be able to point out here that, after Toynbee had made the first anatomical observations on this question, G. J. Jenkins, a Fellow of the Royal Society of Medicine, was in 1913 the first to make clear the same idea and thus to suggest the lines of our subsequent researches.

JOINT DISCUSSION No. 6

Section of Otology and Section of United Services

Chairman—DOUGLAS GUTHRIE, M.D. (President of the Section of Otology)

[February 5, 1937]

**DISCUSSION ON THE EFFECT OF AURAL CONDITIONS
ON FITNESS FOR ACTIVE SERVICE**

Major John Hare: According to Army regulations, all officers and men serving in the regular Army must be fit for active service in any part of the world.

My remarks will be confined to the aural requirements of the regular Army in time of peace; Major Waggett and Mr. E. D. D. Davis will deal with the war aspect.

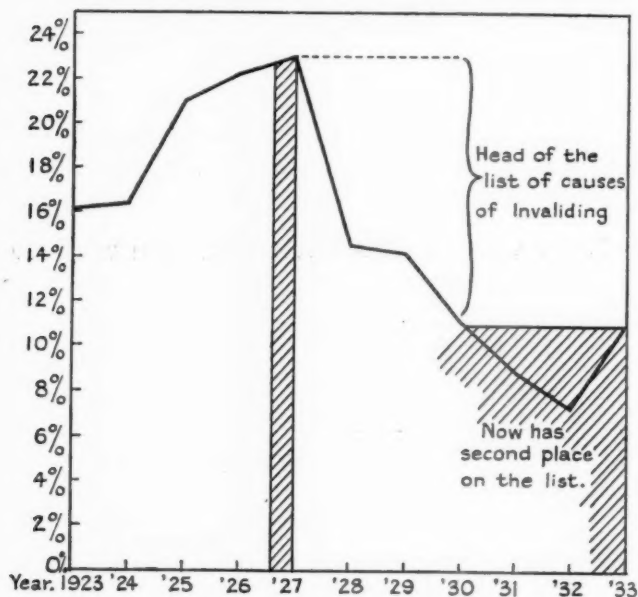
My main object is to attempt to prove by means of graphs and official figures that the present aural policy in the Army, adopted in 1926-27, has thoroughly justified itself by results and, therefore, to recommend its retention.

My purpose can be most usefully served by giving a brief history of the various aural standards in force in the Army since the year 1921. Before this date medical examiners of recruits were only required to ascertain if the hearing was good. In 1921, and because the incidence of aural disease was becoming serious, medical examiners of recruits were instructed to reject any recruit suffering from otitis media or a perforation of the drum. It is necessary to state here that the only instrument then issued to medical examiners of recruits was the non-electrical Brunton auriscope. At this time the electrical auriscope was non-existent.

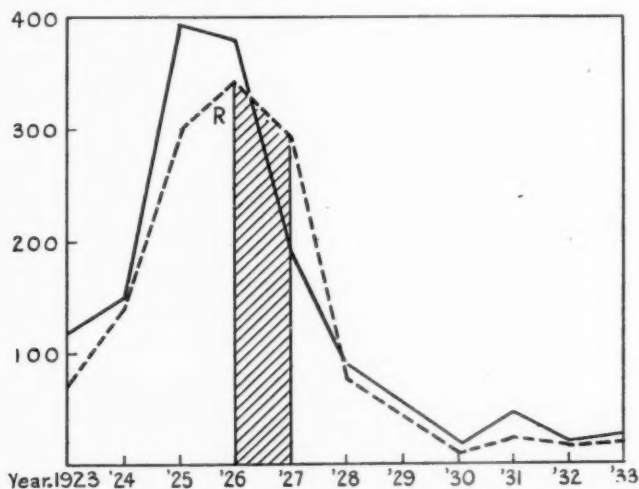
As the aural position in the Army did not improve, but rather grew worse, the Conway Committee was formed by the War Office with terms of reference "High incidence of aural disease in recruits". Graph A shows that from the year 1919 to 1930 aural disease headed the list of main causes of invaliding from the Army, the second place being occupied by tuberculosis. The chief result emanating from this inquiry was that the recruiting regulations then in force were altered to exclude those men who were found to be suffering from a chronic meatal dermatitis, or who had undergone a radical mastoid operation.

Graph B shows that, despite this innovation, the aural position became so serious that during the year 1926 almost 400 men were invalided from India on account of chronic suppurative otitis media. Although this enormous rise was not entirely a true one, it was nevertheless true to the extent that this number of men were discovered to be suffering from this disease in India. Previous to this time it is highly probable that the disease was just as prevalent but fewer men were invalided and a greater number were allowed to serve on.

The aural position still remained a very serious one but had a happy result in calling for a further and immediate investigation.



GRAPH A, showing the percentage of men invalidated annually, suffering from aural disease, of the total invalidated from *all* causes. (Figures provided by the Annual Reports on the Health of the Army, years 1923-1933.)*



GRAPH B, illustrating the total number of men invalidated annually from India, suffering from aural disease. Continuous line—number invalidated to the United Kingdom. Broken line—number permanently invalidated from the Service.

* In all the graphs the period of my tour of inspection followed by the introduction of the electrical auriscope is denoted by the shaded column.

The problem was referred to Major E. B. Waggett, C.B.E., D.S.O. (at that time Consulting Aurist to the War Office) and myself (in the capacity of Aural Specialist to Millbank Military Hospital) by General West, then Consulting-Surgeon to the Army, and we gave it as our considered opinion that the great majority of the cases invalided from India were not cases of aural disease occurring *de novo* in India, but were chiefly in men who had managed to get abroad through evading the aural vigilance of the recruiting medical examiners at home. This contention was fully borne out by the results obtained by me on a tour of inspection of all the depots in the British Isles, in which I examined and reported on the condition of the ears of every serving recruit. In all I examined 8,533 recruits (or 17,066 ears), and of these, 316 men—i.e. about 4%—were found to be suffering from unsuspected otitis media and were at once discharged from the service as unfit (see Table I).

TABLE I.—AURAL INSPECTION OF ALL RECRUITS UNDER SIX MONTHS' SERVICE IN COMMANDS AT HOME.

Name of command	Total number of recruits examined	Number immediately discharged as unfit on A.F.s B204 and B179 inclusive	Number ear-marked for admission to hospital	Total found to be suffering from aural disease	Cases admitted to hospital for treatment			Total Number discharged as permanently unfit	% permanently unfit of total examined	% recruits examined found to be suffering from aural disease
					Number actually treated	Number discharged on A.F.s B204 and B179	Number returned to duty as fit	Number remaining under treatment		
Eastern	3,000	63 (2)	15	78	10	4	6	67	2.2	2.6
Southern	1,713	50 (10)	23	73	23	18	5	68	4.0	4.2
Northern	1,278	60 (2)	37	77	37	13	24	73	5.7	7.6
Western	978	34	26	60	26	12	13	46	4.7	6.1
Scottish	787	41	16	57	15	3	12	44	5.6	7.2
Aldershot	667	11	11	22	8	3	2	14	2.1	3.3
N. Ireland	115	3	2	5	2	1	1	4	3.5	4.4
Totals	8,533	262	130	372	121	54	63	4	3.16	

It was found that the main reason why medical examiners of recruits were failing to detect aural disease, if present, was inadequate instrumentation. The Gallie Committee was then set up by the War Office to consider the situation and my interim reports, and its resultant recommendations were in the main as follows:—

(1) The immediate circularization by pamphlet of all medical examiners of recruits, emphasizing the seriousness of the aural position in the Army and stressing the fact that this position had mainly arisen through lack of care on their part in detecting aural disease, when present, and demanding that more care be exercised in the future. Further, it was stated that their work in this regard would be facilitated by

(2) The universal issue of electrical auriscopes to all those whose duty was or included the medical examination of recruits.

During my tour of inspection one of my chief and most important duties was to demonstrate to medical officers the lesions found and which demanded rejection.

TABLE II.

Year	Total number of invalids from all cases discharged during the year	Number discharged on account of aural disease	Percentage
1923	2,778	451	16.2
1924	2,500	409	16.3
1925	2,152	449	20.9
1926	2,029	454	22.3
1927	2,138	500	23.4
1928	1,661	246	14.8
1929	1,808	260	14.3
1930	1,655	182	10.9
1931	1,487	131	8.8
1932	1,439	112	7.7
1933	1,523	168	11.0

1932 showed a reduction of about 66%.

Graphs C and D and Table II show how immediately effective the above recommendations were and have happily continued to be. In consequence, in the year 1930, for the first time since the Great War, invaliding from aural disease fell from first place to second in the list of causes of invaliding, and has since remained in this improved position.

The combined Graph E (p. 54) is interesting in showing how, as the number of recruits annually rejected at home because of aural disease has risen, at the same time the number of men invalided from the Army from the same cause has fallen.

It is further of interest to examine Graph F, which shows that the number of men constantly sick from diseases of the ears and nose remained at a fairly steady level during the whole period under discussion. As during this period a tremendous number of men were invalided home suffering from otitis media, it is safe to assume that the majority of cases in India are of external otitis rather than otitis media. As in all tropical climates, of course, external otitis is extremely prevalent, and accounts for a great loss of working time and efficiency, through hospital attendance or admission.

It will be generally agreed that the results of adopting the recommendations of the Gallie Committee are very good and striking, as demonstrated by Graph B, which shows that whereas nearly 400 men were invalided from India in the year 1926 there was a fall in the year 1930 to the very low figure of 13, which satisfactory low level is being maintained. This would seem a matter for congratulation, but it must be realized that the present strict aural standard now in force which has brought about this commendable state of affairs results annually in a great loss of potential recruits for the Army, in fact 3,000 men a year, or approximately 6% of the total number of recruits presenting themselves for enlistment (*see* Table III).

TABLE III.—MEDICAL EXAMINATION OF RECRUITS AT HOME.

Year	Number of prospective recruits examined by E.M.O.s	Rejected on account of ear trouble Number rejected on primary examination	Number rejected within 6 months	Total	Percentage
1931/32	54,159	2,773* 220†	284 6	3,283	6.06
1932/33	56,768	2,914* 213†	261 5	3,393	5.97
1933/34	47,392	2,261* 179†	203 4	2,647	5.58
1934/35	45,200	2,202* 167†	284 5	2,658	5.88
Total ...	203,519			Total ... 11,981	

* Diseases of middle ear.

† Other diseases of the ear.

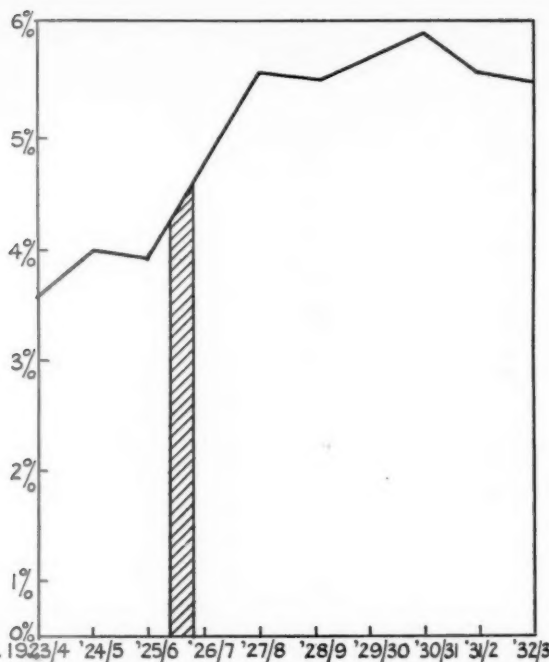
The present aural requirements in a recruit are as follows: A recruit shall not be enlisted who suffers from any of the following defects:—

- (1) Deafness, as defined below.
- (2) Perforation with or without discharge from the middle ear.
- (3) The presence of polypus or granulations.
- (4) Post-aural scar with absence of the drum, indicative of a radical mastoid operation (a simple mastoid operation with healed intact drum and good hearing is no bar to enlistment and all such should be accepted).
- (5) Dermatitis of the meatus (eczematous or desquamative).

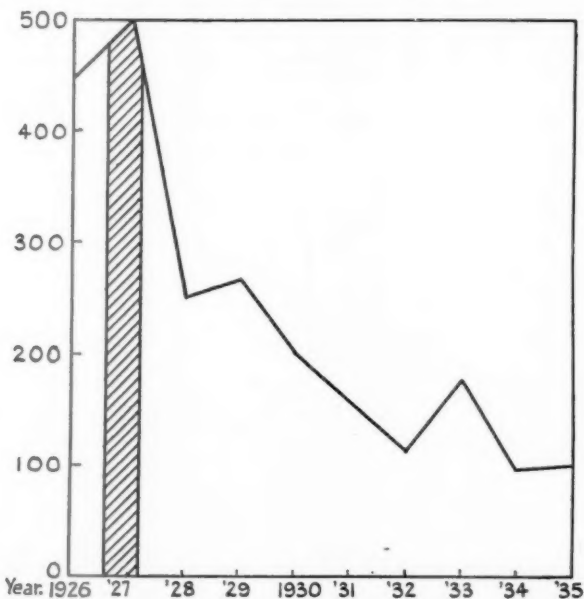
The following will be taken to constitute deafness: Inability to hear with either ear, at a distance of 20 ft., a series of numbers including at random intervals the figures 66 (high note), 25 (medium note), and 44 (low note) uttered in a strong whisper.

The examination will consist of two parts (of which the former is considered the more important): (1) Auriscopic scrutiny, (2) a hearing test, as above.

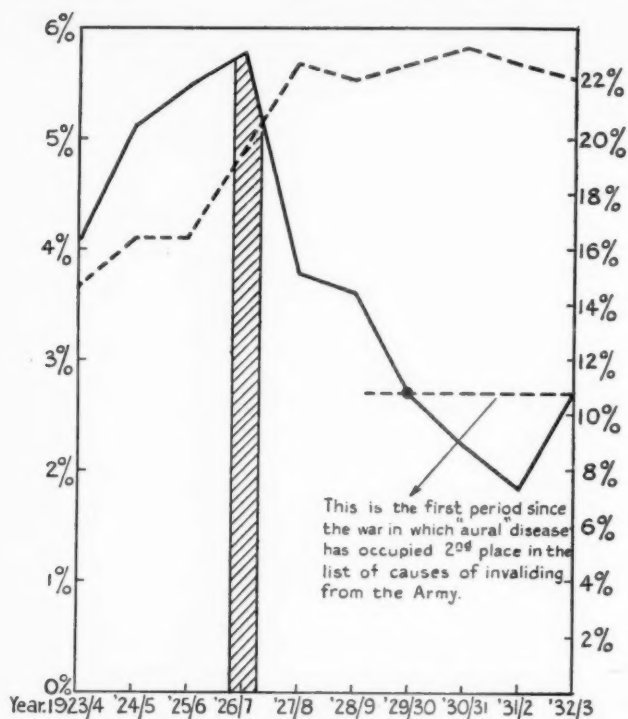
To those unaware of the conditions of service in the regular Army this wholesale rejection of men who are found to be suffering from a perforated ear-drum, but



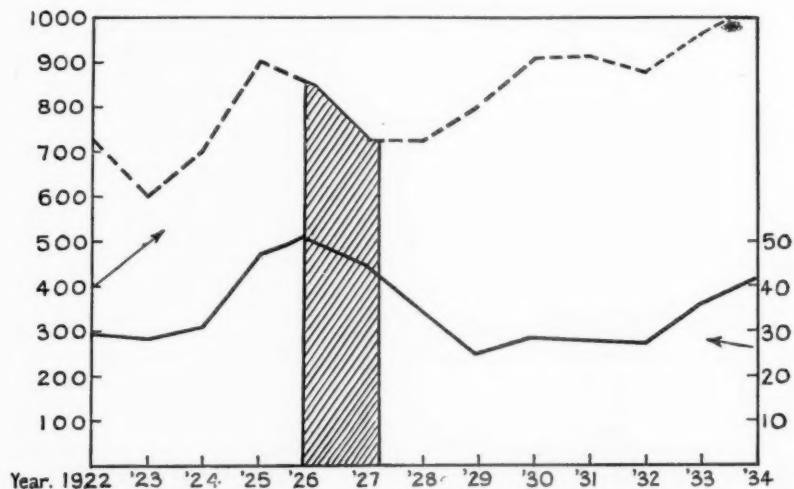
GRAPH C, showing the immediate and sustained rise in the percentage number of recruits rejected on account of aural disease since the date of the War Office Enquiry in 1926-27, and the introduction of the electrical auriscope.



GRAPH D, period 1926-36, showing the great decrease in the number of invalids finally discharged on account of aural disease. Figures for the British Army at home and abroad, including India.



GRAPH E.—Broken line represents the percentage of the total number of recruits presenting themselves for medical examination "at home" who were not accepted on account of aural disease.
Continuous line represents the percentage discharged owing to aural disease of the total number of invalids discharged "from all causes".



GRAPH F.—India. Broken line = number admitted to hospital annually suffering from diseases of the ears and nose.
Continuous line = number constantly sick from diseases of the ears and nose.

who have adequate hearing, would seem to be an act of extreme folly to say the least, especially when it is taken into consideration that these men were found to be otherwise healthy and fit for enlistment. It has, however, already been shown how prevalent external otitis is among troops serving abroad. Given a tympanic cavity vulnerable to infection by virtue of an unhealed perforation, an infection of the tympanic mucosa occurs in the great majority of cases. This re-infection proves very resistant to treatment under tropical conditions and consequently a high percentage of those afflicted are invalided annually to the United Kingdom. This results in the loss of a great number of trained soldiers to the Army and a great financial loss to the State. To a lesser extent the same consideration applies regarding service at home, in that re-infection of the tympanum in the presence of a perforation frequently occurs at bathing parades, which are a compulsory exercise, in spite of measures taken to prevent such an occurrence.

In conclusion, therefore, it is contended that conditions of service being what they are in the regular Army, which requires a man to be fit for service in any part of the world, the present aural standard should be adhered to and that, although it might be criticized as being too strict in its requirements, results have amply justified its adoption and retention.

Mr. E. D. D. Davis: The decision as to whether a recruit with any aural defect should be accepted depends on a number of other details apart from the actual condition of the ear. There can be no hard and fast rule, and every doubtful case has to receive individual consideration. A private is a recruit for six months, and if at the end of that period he is physically suitable and fit, he has to serve for seven years with the colours and five years on the reserve. If a private wishes to leave the Army after the recruiting period, he either has to be declared unfit by a medical board, or he may be able to buy his discharge. The cost of training and equipping a recruit is approximately £50, and if he is then found unfit or if he has to be sent home from foreign service, a considerable loss is sustained.

It is therefore important that the ears and hearing of every recruit should be examined for any defect which might make him unfit. A recruit who joins the Army for lack of something better to do is more likely to make the most of a defect, while the keen intelligent soldier who has selected the Service as a career will do his best to conceal or overcome any defect, and he will not report sick when detailed for service abroad or when he is disappointed with his job. For this reason, a defect in an officer is of less importance than a similar one in a private, who may be pressed by force of circumstances to enlist. When the demand for recruits exceeds the supply, i.e. during war or threatened war, small defects of the ears would be ignored and recruits who would be rejected in peace time might be accepted. Again, the unit and type of service has a considerable influence; a recruit for the Army Pay Department, the Service Corps, or the R.A.M.C. may be accepted for clerical work, but would be rejected for fighting service. It is probable that no recruit with any defect in his ears would be accepted for the Air Force. Major John Hare, with his long experience of ear-nose-and-throat work in the Army, is much better qualified than I am to indicate those defects of the ear which should or should not reject a recruit, but I will give my own experience briefly on this point.

Firstly, recruits with chronic suppuration, or cholesteatoma which cannot be cured by treatment, should be rejected.

A candidate who has had a radical or conservative mastoid which has healed, owing to the defect of hearing and other reasons is not a good recruit for a fighting service. In the Great War I happened to visit a stationary hospital in France during a lull in the fighting, and in one ward there were no less than twelve mastoid cases which

had been operated on for chronic suppuration. It is true that the surgeon was an aurist in civil life, but it was a strong indication to me that a man with chronic suppuration cannot stand up to the strain of war. This is also emphasized in those cases which have a neck scar as the result of tuberculous glands in early life. This type of case in my experience has little resistance to pyogenic and catarrhal infections. There is one type of suppuration which may be accepted, and that is the large perforation of the lower half of the drum, with no active disease but only an occasional mucopurulent discharge during a cold, in which the hearing is only slightly diminished.

There is a difference of opinion as to whether men with otosclerosis should be accepted. Stress and strain and loud noises increase the deafness, but during the War some cases of otosclerosis were accepted, particularly as service was only expected to last from three to five years. Men with otosclerosis may be accepted for short service, but not otherwise. Vertigo is, of course, sufficient to disqualify.

It is suggested that a recruit with an unimportant defect of the ear should be accepted if he will give a guarantee that he will not claim compensation if the defect is increased by service, but it is highly improbable that this undesirable guarantee could be sustained in law.

Group Captain David Ranken: Nine years ago as the representative of the Royal Air Force, I opened a joint discussion on a subject similar to the present one. Its title was, "The effects of middle-ear disease on efficiency in civil and military life".¹ Practically everything I said then is relevant to this discussion, but I will try to emphasize the points in a different way, and bring them up to date.

The effect of aural disabilities on fitness for active service must depend entirely on what the active service conditions are, and what degree of aural fitness is necessary to cope with them satisfactorily. In the Royal Air Force, our aural recruiting standards, both for flying and ground personnel, have always, with certain slight relaxations, been definable by the four words "Nothing but the best". We have been able to carry out this policy because ours is an attractive service and the supply of recruits, both for flying and for ground duties, has always been equal to the demand. On the other hand, in the case of officers and men already in our service, we recognize such grades as: Fitness for full flying duties, fitness for limited flying duties, fitness as a combatant passenger, and fitness for ground duties. All four categories are either for general service or for home service. As a temporary recruiting measure, we have recently introduced a Grade II for G.S. or H.S., based on slight hearing defects, but limited to ground duties. So far, we have not relaxed our aural recruiting standards for flying duties, but in time of war I think we would do well to modify them. It will thus be seen that the system of grading, which has recently acquired prominence, is nothing new to us; further, we have always recognized that peace standards might have to be modified in time of war. May I therefore briefly indicate the broad principles on which I would grade recruits suffering from aural disabilities, either when the supply is less than the demand, or, in the case, say, of a national emergency when nearly everyone would be called upon.

I would have no objection to passing the milder case of meatitis as fit for active service; I know that dust and bathing often aggravate the condition, but I think that prophylaxis and treatment would prevail in most cases, so far as fitness for duty is concerned.

The effect of chronic suppurative otitis media on fitness for active service must be an extremely varied one. We all know the possible complications, e.g. recurrent earache, deafness, tinnitus, and vertigo; we also all know of many cases in which symptoms or signs have been slight or absent for—at any rate—two years. I.

¹ *Proceedings*, 1928, 21, 1455.

personally, would be prepared to accept for ground duties on active service, most men in the latter category. For flying duties, either at home or abroad, the case is rather different, as symptoms of apparently trifling importance on the ground may become considerably aggravated in the air; engine noise, for example, aggravates tinnitus and abnormal movement aggravates vertigo; we lay it down, however, that although a permanent perforation, generally speaking, constitutes a disqualification for flying, yet a candidate may be passed, provided the examiner is satisfied that the condition is unlikely to prove a disability and no active disease is present. For ground duties on active service I would reject men suffering from chronic suppurative otitis media complicated by exacerbations, those whose hearing is not reasonably acute, and unlikely to improve, and those who suffer from tinnitus and vertigo. I believe that the effect of these conditions is to limit very considerably a man's fitness for active service; such people cannot be employed as sentries, do not readily grasp verbal instruction, often figure on sick parades, and have opportunities for malingerer. I described the advantages of rigorous standards of recruiting—both to the Services and the State, and from the point of view of fitness for active service—very fully, in the 1928 discussion, so that there is no need for me to go further into this aspect of the situation this evening.

We will presume that it is necessary to accept large numbers of men suffering from aural disabilities, or that such men have eluded the vigilance of the recruiting examiners, and have to be retained, if possible, in the Service; what will happen—especially on active service?

The same thing will happen that always happens when medical standards are lowered; more beds, more hospitals, and more medical officers with otological training will be needed, both at home and abroad; provided they can be obtained, we may then perhaps be justified in accepting men with aural disabilities; if such men cannot be cured, they can often be patched up by treatment, when the severity of the symptoms becomes a disability. It seems to me incontrovertible, however, that a man who is sound and healthy in all respects is more useful and successful on active service than one with any physical defects which limit his activities.

There is one further observation I should like to make. Perusal of Health Reports for the last few years leads me to believe that a different type of recruit presents himself for the Royal Air Force than for the Army, at all events from the aural point of view; the Army appears to be obliged to reject more recruits per cent. than we do for aural disabilities, and also to invalid more per cent. It would be a great boon, therefore, if the health services of the country could reduce the large amount of chronic aural disease that seems to exist amongst our young population. To me, one great advantage of a joint discussion like this is that it enables Service otologists to explain recruiting difficulties to their confrères in civil life; we can ask them, not merely to treat aural complications as they arise, but to push forward by every means in their power, schemes for the prevention or early treatment of aural affections, long before they become chronic disabilities.

Mr. Terence Cawthorne: I should like, briefly, to discuss functional tests of hearing and their part in determining the fitness of candidates for Service life.

Because of the great increase in the extent of the communication and detection of sound following the invention of the wireless valve, efficient hearing is of greater importance in Service life than ever before. Under modern Service conditions the ear may be required to detect and distinguish different types of engine noise, and also to pick up relatively weak speech sounds or signals when imperfectly insulated against loud background noise. These are but some of the conditions that make an increasing demand on the auditory apparatus. This calls for a high degree of hearing in candidates for Service life and for some duties, notably flying, communications, and sound

detection, the hearing should be perfect. This is of course fully realized, and from information kindly supplied me by the Directors of the Medical Services I understand that particular attention is paid to the condition of the ears, nose, and throat.

The tests of hearing capacity usually employed include the acoumeter, conversational and whispered voice, and in certain circumstances three tuning-forks—of low, medium, and high pitch, respectively. These tests should, and do, reveal most hearing defects, but they suffer from certain drawbacks, namely :—

(1) The voice tests call for the greatest care in technique if results of value are to be obtained. (2) It is wellnigh impossible to standardize the human voice, and therefore the results may vary considerably from examiner to examiner. (3) It is difficult to get standard conditions for their repetition, even if carried out by the same examiner. (4) It is not easy to classify and tabulate the results. (5) It is possible for minor degrees of hearing loss, and also for islets of deafness, to escape detection. (6) A well-schooled candidate may be able to acquit himself unduly favourably and—what is equally, if not more, important—a reluctant recruit, even if suspected, may be difficult to expose with these tests.

Is there any way in which functional tests of hearing can be made more standard and, if required, more searching, without at the same time increasing the technical difficulties and time of the examination ?

The audiometer seems to me the ideal way of estimating the hearing capacity, either in groups or individually.

For individual testing the pure tone audiometer enables a candidate's hearing capacity for a range of tones—say eight at octave intervals—to be compared with an accepted normal. Any hearing loss as compared with the normal can be expressed in definite units (decibels) or as a percentage, and the result expressed in graph form. By these means a chart of the whole auditory area (known as an audiogram) can be prepared in little more than five minutes. What is more important, this examination can be safely entrusted to a technician or trained orderly.

For group testing of recruits, in which such a detailed examination may not be required, the gramophone audiometer can be used. With this as many as 40 recruits can be tested simultaneously. This relies upon a gramophone record of a voice speaking combinations of numbers at different intensities, the decibel value of which is known.

There is no doubt that the audiometer furnishes us with accurate and valuable information as to the hearing capacity in the shortest possible time. In describing the merits of the audiometer I do not wish in any way to detract from the value of the time-honoured voice and tuning-fork tests, or to suggest that they should be dispensed with. I want, however, to emphasize that the voice as a test cannot be accurately standardized. Although it is undoubtedly the most valuable test for speech interpretation, it cannot claim to be anything but a rough test of auditory acuity. As regards tuning forks, they can give an accurate picture of the whole auditory field, but their use calls for considerable technical skill, favourable surroundings, and takes a long time. The audiometer, however, is less dependent upon the human factor; the tests are more easily carried out; it is more difficult for minor degrees of deafness to escape detection; and it is easier to check the replies of possible malingerers. The audiogram portrays a correct measure of any loss of hearing over the whole auditory scale; it can be produced in a standard manner by any technician in a relatively short space of time; and it serves as a permanent record of the hearing capacity for comparison with future tests. There is not, I think, any doubt of its value as a test of auditory efficiency, but it may be said that in these days when the demand for recruits exceeds the supply, more searching methods of testing are not required. However, the additional information obtained from an audiogram will, without

necessarily raising the standard of entry, afford added assistance to the medical examiner when assessing candidates. Also, in cases of hearing defects resulting from active service, a medical board would be able to refer to previous audiograms in assessing disability.

Surgeon Lieut.-Commander V. G. Horan: Aural fitness for active service in the Royal Navy may be considered from two different points of view. Firstly as to the effect of aural disease or disability on personnel already serving, and secondly as to its effect on candidates for entry.

I have no personal experience as a recruiting medical officer, but from time to time I have to consider the question of invaliding as "unfit for service" cases of aural disease or disability which arise in the active service personnel. The facts governing one's decision in these cases are, with some modifications, the same as those considered by the recruiting medical officer when examining new entries. The official standard of fitness for both active service personnel and for candidates for entry is 100%. There are, of course, men with aural disability or disease who are accepted for the Service or whose services are retained when such disability or disease does not—and is considered unlikely to—interfere with their efficiency as officers or ratings. This question is bound to be influenced considerably by the urgency of recruiting. At present, in the Royal Navy recruiting is good, and consequently the standard of aural fitness for recruits and active service personnel is high, but when recruiting is bad or when a large increase of personnel is required, as in war-time, the standard must of necessity be lowered. The degree of leniency in this respect is to a large extent dependent on the recruiting medical officer.

In the Royal Navy we deal mainly with male patients ranging in age from 16 to 50 approximately, who presumably, in most cases at any rate, were 100% aurally fit when they started their Service career. This probably reduces very considerably the number of aural cases met with compared to those which arise in civil life in male patients of the same age—the type of case however is probably much the same. We are not concerned at present with those cases which clear up satisfactorily with treatment, but rather with the fate of the chronic cases and those with resulting disabilities.

From the point of view of invaliding these men or of rejecting them as recruits, several questions have to be considered, the main one being whether the efficiency of the officer or rating is likely to be impaired in his present, or possible future, occupation, and whether it is likely to interfere with his training and necessary swimming instructions. We endeavour, in the case of recruits, to have any nasal trouble, infected tonsils, dental sepsis, &c., treated previous to admission, but in some cases these are dealt with subsequently if not sufficiently gross to cause rejection in themselves. We also have to consider the degree of disability present and whether it is likely to be stationary or progressive, as a stationary minor disability is not, I think, in some cases a sufficient ground for rejecting or invaliding. The rank or rating of the patient has also to be considered, together with his length of service, and the degree of skill and training which he has acquired and its value to the Service. With the more senior officers and ratings, whose skill and training may be of great value to the Service, a greater degree of leniency is exercised. In some cases there are opportunities to transfer active service personnel from one branch of the Service to another in which the disability may not interfere with their efficiency, or to classify them for drafting by keeping them under some drafting restriction—for example on home service or close to medical supervision.

I do not think that men who have undergone a radical mastoid operation, or who require one, should be considered for entry or for retention except in very special circumstances. With regard to the cortical mastoid operation with a good result

the case is different, and personally I do not think that in these cases the men should be either invalided or rejected. We must, however, keep as near 100% fitness in peace time as recruiting will permit. In recruiting we deal with men as yet without training and consequently of less value to the Navy, so that less leniency is to be expected. Men with dry perforation of the tympanic membrane, though quite fit for civil life, often break down under Service conditions in the tropics or under necessary swimming instruction, and consequently are not suitable cases for entry. Another type of case which I consider to be unfit in many instances is the chronic otitis externa—and for the same reason.

Our peace-time Service is the nucleus of what our war-time Service will be, and every effort to keep it as near 100% fit as possible has to be made, especially in the more specialized branches. The decision for rejecting candidates rests to a large extent with the recruiting medical officer, who knows the type of work the men will be required to do in the various branches of the Service and who assesses the fitness of each candidate.

Major E. B. Waggett: I shall confine my remarks, in the main, to ear conditions in an army on active service; if my thesis is maintained, details of army recruiting regulations for national emergency follow as a rational consequence. And I speak as a soldier—that is to say I do not regard a period of active service as a suitable occasion for the performance of operations and elaborate treatments proper enough in peace time. The function of a medical officer in war is to keep fighting units as near up to strength as in him lies.

I shall attempt to show that the prominence accorded to ear disease in the Army of 1914–18 was quite unnecessary and grossly exaggerated, and this was owing to the fact that medical officers were unfamiliar with the elements of otology and anticipated grave complications in all cases of otorrhœa. In any future national war we may look forward to a much more favourable state of things, for otology has now become compulsory for the qualifying examinations of the R.C.P. and the R.C.S., while the largely increased numbers of genuine aurists should supply an expert, at least, to every casualty clearing station.

The aural invaliding and recruiting crisis into which Major Hare and myself were detailed to inquire a few years ago was really a financial affair and somewhat different from our present problem, but certain points in Major Hare's results are worthy of special notice here. Of genuine ear cases, 90% of the men heard quite well on parade. In a certain year, India sent back invalided 404 ear cases. They were nearly all old perforation cases with mucopurulent catarrh set up by Service conditions, notably by compulsory bathing. It was then arranged that no man with a perforation should bathe without an ear-plug and a subsequent visit to the unit inspection room for the instillation of biniodide and spirit drops. The invaliding dropped to 13, and has remained thereabouts. The most important point for us in Major Hare's report is that if all applicants with ear trouble were rejected by the recruiting medical officer, we should lose at least 6%—he estimated at the time that the figure would be 10%—of the total applicants. In recruiting on a national scale we cannot afford to reject anything like that percentage merely for ear trouble, nor is there any necessity to do so, as I hope to show. For pension purposes a record of aural defects should be made at the time of recruiting.

My own experience is that of an aurist with twenty years' civil hospital practice, acting for four years as an executive officer in a field ambulance, and therefore in touch with the fighting formations. In 1915 a field ambulance was a big affair, in our case (85 F. A., 28 Div.) occupying a great building, and alternately with one sister ambulance taking in all cases from half the Ypres salient, often from 400 to 1,000 a

night, and retaining large numbers until their return to the firing line ; for we had some first-rate surgeons and physicians among the officers.

After several months of this service I received an unofficial letter from the Statistical Office asking how I explained the enormous influx of ear cases to the base. I replied that I was amazed at the query, for I had seen no single ear case worthy of sending down the line—and the wet trenches round Ypres were no health resort !

At the end of 1915 the division went to the Balkans. There the field ambulance served 6,000 troops, often retaining 500 sick cases from start to finish ; sending them back after convalescence to their units. During three years of that service we sent down exactly two ear cases—one, after a hurried glance, just before a battle, and one for vaccine treatment against recurrent furunculosis. Every day a corporal would be seen treating three or four cases of catarrhal discharge and sending the men off to their units with drops or powders, to return in a week ; a loss to the force of say, twelve hours in all, spread over four weeks.

During a period of about six months, in the absence on sick leave of the throat-and-ear consultant, I went down to Salonika once a fortnight to help the eye consultant who had taken over the department. During that period I operated on one doubtful mastoid, a case which, as it proved, required no operation, but I did not care to leave it until my next visit.

I have related the four years' experience of active service in two remarkably unhealthy terrains—the experience of an aurist, that is to say, of a medical officer who recognizes in discharging ears the immense difference between an antero-inferior perforation and one in the postero-superior quarter. Is it too much to ask to-day, that every field ambulance should have one officer capable of making this easy distinction ? Experience of 1917-18 tells us that we cannot afford in national emergency to reject recruits for slight defects, and all aurists will agree that old perforation cases under exposure will from time to time show a discharge which clears up in about three weeks, with the simplest conservative treatment in the case of antero-inferior perforations. Every civil out-patient room holds numbers of such cases daily, but the subjects do not dream of going sick and stopping work. Some such cases urgently need pharyngeal or nasal interference. In point of fact, I did not see one such case during the four years.

Also I would urge that there should be a genuine throat-and-ear specialist at each casualty clearing station. He will get very little important ear practice, but he can make himself quite useful in other ways. He can tie arteries and cut off limbs quite efficiently, and his experience of cranial surgery will probably exceed that of his brother officers. In the German push of 1918 I served in a C.C.S. in France for some weeks, and three or four head cases were detailed to my operating table every night. An aurist in a C.C.S. will prevent these mild ear cases getting past railhead to the base. I think all front-line medical officers will agree that once a man gets to the base they will not see him again for two months ; he will come back soft, undisciplined, and lacking *esprit de corps*, and it will take a further three weeks for him to shake down again. The authorities need not fear aural pension troubles if records are taken in the recruiting office. Drumheads ruptured by explosion are best left strictly alone, while cochlear concussions gain nothing from the aurist.

As I have been privileged in the past to advise the Army Medical Department on aural regulations for peace-time recruiting, may I make some suggestions for mass recruiting in national emergency ?

That hearing of forced whisper at 10 ft., with the back turned to the examiner, should suffice for general service.

That an inspection of the drumhead should be made in all cases ; an interval of half an hour should elapse after syringing for wax. The electric auriscope facilitates examination for medical officers unused to the forehead-mirror.

That a man with aural discharge, whether meatal or tympanic, should be directed to a civil hospital, to return in two months for re-examination.

That all candidates with dry perforations should be accepted for general service, provided the perforations are not in the postero-superior quarter.

That otherwise desirable applicants who have dry postero-superior perforations (i.e. free from granulations) should be accepted for permanent base (where they will do just as well as in civil life).

That in conservative mastoid cases with healed drums and at least six months' "dry" history, the men should be accepted for general service, and that in radical mastoid cases with twelve months' "dry" history, they should be accepted for permanent base.

That men with intact drums but with defective hearing, tinnitus, vertigo, or paracusis, should be examined by an aural specialist, as a precaution in regard to pensions.

That cases of atresia and of marked hyperostosis should be rejected.

That all functional or structural ear defects in men accepted should be recorded as a pension precaution.

Dr. Bernard Potter said that he had had experience of the generality of medical cases in the Great War, from early in 1915, in Flanders, to the end of 1918, in Salonika, so that he had obtained a good idea as to the average kind of case. Throughout that period the ear cases did not make a great impression upon him. Bad cases of pneumonia, typhoid, &c., were not likely to be forgotten because of the anxiety that they had caused, but he had not encountered any ear cases which caused a comparable anxiety. He did not think that great disability in war-time need be anticipated from ear troubles. He would not encourage a practitioner intent on specializing in ear diseases to expect much experience in this respect in war-time.

Mr. W. J. Harrison said that only those men whose ears were not affected in any way should be accepted as recruits for the Services; those who had either perforations or incipient deafness should be rejected. During a war, however, it was unreasonable to expect those responsible to worry over small defects, and he agreed that men should be kept in the line as long as possible. For more than twenty years he had been a territorial regiment medical officer, and he had taken the greatest care when examining recruits to reject all the ear cases.

He had been present in the Ypres salient mentioned by Mr. Waggett in the spring of 1915, and he agreed that there had been a great shortage of men; one could not send men down because they had a running ear, and so leave the battalion weaker still. There was no reason why such men should not be retained in the line if their ears were reasonably looked after. He had seen a number of men with running ears who were having a good time at the base when they might have been usefully employed. Later on many of those men would claim pensions—a source of great expense to the country. During a war, running ears should not be regarded too seriously in the field.

Mr. Philip Jory said that there was one point of great importance to aurists. Occasionally one saw a boy who had acute suppurative otitis media, and in whose case one considered a cortical mastoid operation necessary. The question asked of one was as follows: "My boy wants to enter the Army" (or the Navy, or the Air Force), "if he undergoes this operation will he be accepted?" In such a case, if there was complete healing of the drumhead and, apparently, perfect hearing, would the youth be accepted as a cadet in one of the Services?

Major Hare (in reply to Mr. Jory) said that the Army accepted recruits who had had a simple mastoid operation performed, provided that the hearing was completely restored and the drum was intact. The Army did not accept a recruit who had had a radical mastoid operation, even if the hearing was up to the required standard.

Mr. C. S. Hallpike asked whether any set tests had to be used for testing Air Force men whose work would consist of listening, sound-localizing, and work of that description.

Group Captain Ranken (in reply to Mr. Hallpike) said that a more thorough and detailed examination was made in the case of men who had special duties to perform, and for whom first-class acuity of hearing was essential. In addition, more audiometric examinations would be made in the future, which, he hoped, would add to the reliability of the tests.

Surgeon Rear-Admiral J. Falconer Hall said that during the War he had had a hospital ship at the Dardanelles and other bases, and had evacuated more than 6,000 men. He did not remember having seen a mastoid operation performed on the ship. The number of ear cases among those evacuated was quite trivial.

Mr. F. C. Ormerod said that he wished to raise two points. The first referred to the condition of the nose, the accessory sinuses, and the nasopharynx, in recruits. The occurrence of catarrhal changes in the middle ear, or of suppuration, might be influenced by sepsis in the nose, or obstruction caused by a deflected septum or by polypi. To eliminate waste as far as possible it seemed important to examine as to those conditions in recruits. Not only was the chance of suppuration increased by such obstruction in the nasal passages, but it was certain that the damage done by explosions was greater in those men who had obstructive disease in the nose and nasopharynx.

His other point also had reference to recruiting. At the beginning of the Great War he had helped to examine recruits, and attention had been given to height, weight, colour of eyes, &c., all those particulars being carefully recorded, but no examination of the ears was made; ears were not looked at, or, apparently, thought about. During the War there was little acute ear disease, or only a few complications. His own service had been almost wholly with Indian troops, and among them he had seen only one case of acute mastoiditis. After the War, however, a very large number of discharged soldiers were seen, having a purulent discharge from the ears, and these cases cost the country an enormous sum of money; the men were granted pensions and were given treatment for a number of years. Yet there was no record of defective ears in these cases when the men had joined the Army. If the ears of the recruits had been examined, a large proportion of that expense would have been avoided, as existing aural disease would then have been noted. In a certain number of cases there was an aggravation of the ear trouble due to war conditions.

Mr. G. Ewart Martin supported what Mr. Ormerod had just said. Now that there was to be a classification of recruits it should be possible to enter on the form the condition of the recruit's ears and his hearing capacity. He saw many Ministry of Pension cases in Scotland, and he was alarmed at the conditions which

had been missed before the recruit was accepted for service. That referred especially to otosclerosis, which must have been present in some form in the men before the War, especially the men who were taken on after the end of 1916.

Another point he wished to raise was whether it would not be possible for the recruiting authorities in the Army, Navy, and Air Force to issue instructions on this matter to those in charge of ear and throat departments of hospitals in bigger centres. Men were referred to large centres from recruiting stations with the request: "This man is suffering from a discharging ear, or pure otitis externa; can you make him fit for service?" Also, if there was to be a classification, could one know whether one was to accept anterior perforations, which were accepted by insurance officers as A1?

Mr. Sydney Scott agreed with the suggestion that records should be kept of the ear conditions in recruits for reference later, for as Mr. Ormerod had said, the country would have been saved large sums of money being paid for what were really pre-War disabilities, had this precaution been adopted in the Great War.

The importance of the investigations which Major Hare had carried out was officially recognized, and it was hoped that the increase in the number of medical officers trained to examine ears, would enable the authorities to meet the omission in future.

In the later stages of the Great War the authorities had appointed officers with aural experience to be near the front lines, because during or after an engagement large numbers of men had found that they had only to complain of deafness, or earache, or show discharge from the ear, to ensure being sent down to the base. These otological experiences were related in his (Mr. Scott's) contribution to the "Official Medical History of the War".

The Chairman said that he was interested in this subject in his capacity as Aural Consultant to the Scottish Command. A year ago he had analysed the results of nine years' work, of which he had fairly complete records. There were 3,000 new cases, and about one-third of these were cases of middle-ear suppuration. He had also investigated various Reports of the Army, so as to have larger figures to compare with his smaller ones, and in that comparison he had found some interesting facts. He had discovered that, as a cause of admission to hospital, inflammation of the middle ear ranked twentieth on the list, influenza taking first place, and malaria second.

With regard to recruiting for the Army, many recruits were rejected because of obvious defects before they reached the medical officer at all. Some 50,000 recruits were examined for the Army each year, and 67% of them were rejected at sight. Of the remainder who were provisionally accepted and sent up for medical examination, 35% were rejected, the chief cause of that rejection having been middle-ear suppuration (*see* Table I).

TABLE I.—PRINCIPAL CAUSES OF REJECTION OF RECRUITS ON ENLISTMENT OR WITHIN SIX MONTHS (1931-1934).

	1931	1932	1933	1934
Diseases of middle ear ...	3,680	3,057	3,175	2,464
Loss or decay of many teeth ...	2,260	2,460	2,764	2,162
Defects of lower extremities ...	2,509	2,402	2,494	1,702
Total number rejected	22,157	21,326	22,638	16,935

Chronic suppurative otitis accounted for the rejection of 50 recruits out of every 1,000 who applied for admission to the Army. In this way the country lost about

3,000 recruits a year. Table II showed the incidence of middle-ear suppuration in the Scottish Command, and the gradual fall which resulted from greater care in examination and the more general use of the electric otoscope.

TABLE II.—INCIDENCE OF MIDDLE-EAR SUPPURATION IN SCOTTISH COMMAND 1931—35, AND EFFECT ON FITNESS FOR SERVICE.

	1931	1932	1933	1934	1935
Total cases of middle-ear suppuration	113	96	69	50	46
Acute suppurative otitis (practically all subsequently fit for service) ...	45	36	29	16	14
Chronic suppurative otitis ...	68	60	40	34	32
Number of chronic cases unfit for service	39	25	28	34	27

The table also showed that acute suppurative otitis media was nearly always cured by treatment, and the man became fit for service. The number of these cases varied from year to year; at the present time they were on the downward grade.

With regard to chronic suppurative otitis, the number recorded as unfit varied; in 1931 there were 68 cases, and 39 of these were regarded as unfit, but all the 34 cases in 1934 were considered to be unfit, the reason being the appearance of a graver type of case, not amenable to treatment. Some of the cases seen in 1931, though of chronic type, were rendered fit by treatment.

The trend of opinion expressed in this discussion was that one must look upon the two classes—(1) the recruit, and (2) the man who had been in the Service a considerable time—from different angles. With the recruit the examiner should be very radical; the recruit must be as fit as possible, and if the numbers applying were sufficient, a high standard must be maintained. Under war-time stress, however, it might be necessary to accept for service a certain number who in time of peace would have been rejected. Towards the man who had been in the Service for some time or who, at the time, was taking an active part in warfare, the attitude of the examiner would be conservative. One would hesitate before rejecting a veteran for an ear defect which might disqualify a recruit. One would be even more disinclined to invalid a man occupying an office position, or one who had been trained to carry out some special technical duty; or, to take a concrete example, a man who was discovered in routine examination to have a perforation of the drum, with slight deafness, and who had, say, fifteen years of service to his credit, and did not wish to leave the Army but was anxious to finish his time. It would be wrong to invalid such a man when he was not making any complaint about his ear condition.

With regard to the ear cases which turned up actually during a war, one must avoid sending numbers of men down the line to the base because they had discharging ears if the ear trouble was not rendering them unfit for their duties.

Major Hare (in general reply) said that many cases referred to his colleagues and himself were of the type in which examination had revealed that disease, of either a catarrhal or suppurative kind, had affected the ear or ears at some time during childhood, and in which a possible causative factor or factors was still present in the nose, throat, or postnasal space; the custom was to tell the recruit that if he underwent the necessary operation at his civil hospital he would be accepted when he again presented himself for examination, i.e. after tonsillectomy or the removal of adenoids or nasal obstruction. This practice had, of necessity, resulted in the loss of a few recruits, because only the keen recruits would undergo operation. However this loss was not serious, as the total number in this category was small.

Surgeon Lieut.-Comdr. V. G. Horan (in reply) : With regard to the subject of compensation following discharge, the candidate for enlistment in the Navy is required to sign a statement as to whether or not he has ever had any discharge from his ears. If he subsequently reports sick with any aural condition which is considered to have been due to active service conditions or occupation, he is granted a Hurt Certificate on which is described the nature and cause of his condition, and a notation is made on his medical history sheet. Compensation is subsequently assessed, in the light of this notation, on any resulting disability. In the absence of such a Hurt Certificate or notation on his medical history sheet, the condition is considered to be constitutional, and for that he receives no compensation.

JOINT DISCUSSION No. 7

**Section of Epidemiology and State Medicine
with Section of Medicine**

Chairman—Surgeon Rear-Admiral SHELDON F. DUDLEY, O.B.E.
(President of the Section of Epidemiology)

[May 28, 1937]

DISCUSSION ON AIR-CONDITIONING

Ventilation Conditions and their Investigation

By ROBERT C. FREDERICK, F.I.C.

(Royal Naval Medical School, Greenwich)

I WILL confine my remarks to ventilation conditions as affected by, and as affecting, human habitation, and to methods of investigation in general use.

My experience has been gained in H.M. ships and naval establishments. In H.M. ships living space is limited, and cannot be otherwise, and the provision of ventilation adequate to counteract this receives attention in an especial degree. All matters relating to the investigation of ventilation conditions are centralized at the Royal Naval Medical School, Greenwich, to which samples of air and appropriate records are forwarded. In various circumstances it is necessary to examine conditions *in situ* and on such occasions a transportable laboratory is employed. This laboratory is completely equipped and self-contained, and is ready to function in any situation in which it may be placed.

Carbon dioxide as an index of respiratory impurity.—The first matter to consider in ventilation is its relation to the prevention of the spread of air-borne disease. It will be accepted, perhaps, that if the degree of respiratory impurity in the air of a space is maintained at a minimum there will be less risk of organisms from a carrier becoming established in a new host.

Fresh air contains 3 to 4 parts of carbon dioxide per 10,000 and expired air about 400 parts, so that a determination of the carbon dioxide present furnishes a reliable index of the degree of respiratory impurity. It has been recommended that a permissible maximum of 12 parts of carbon dioxide per 10,000 should be allowed. In the light of the records of all the factors which have to be taken into

consideration, obtained in the investigation of conditions in some thousands of spaces, I think this is too high, and that anything over 9 should be regarded as unsatisfactory.

I would emphasize that the carbon-dioxide figure is only an index, and that this amount of carbon dioxide is quite harmless. Indeed, if the carbon dioxide in the air of this hall were increased to 200 parts per 10,000, I doubt very much whether anybody would notice it. Even with 250 parts per 10,000 there is little effect, though you might be surprised and perplexed to find that matches, after the initial splutter of the head, refused to burn. It is only when the carbon dioxide exceeds 300 parts per 10,000 that the effect is really appreciable, and there is an acceleration of the effect with higher concentrations; to live in an atmosphere in which the respiratory carbon dioxide has attained 500 parts per 10,000 is an experience of which one is likely to retain a vivid memory.

For the estimation of carbon dioxide the apparatus employed is the one devised by Professor J. S. Haldane, and also a modification of this to enable amounts up to 500 parts per 10,000 to be determined.

Oxygen.—A determination of the oxygen is very seldom necessary. When the deficiency is known to be due entirely to respiration a close approximation is obtained by multiplying the carbon dioxide by the factor 1.1; this figure subtracted from 20.95 gives the amount of oxygen present. So long as the oxygen is not less than 17.5 per cent. the amount is without physiological importance. When a determination is necessary the Haldane general air analysis apparatus is used.

Measurement of air supply.—If the carbon dioxide is excessive this indicates that the dilution of the respiratory impurity is insufficient, owing to the fresh air supply being inadequate, and it may be necessary to measure the amount actually entering the space. If the supply is artificial, by means of a fan and trunk, the most accurate method of making this measurement is by a Pitot tube attached to a differential liquid or a slope gauge. This involves a large number of readings and calculation. The result obtained is the velocity of the issuing air in feet per minute, and this multiplied by the cross-sectional area in square feet gives the volume of air in cubic feet per minute. The velocity determination can be made accurately enough for most practical purposes by means of an air meter. An initial reading is taken, and then again after the instrument has been in the air-stream for half a minute or a minute timed by a stop-watch. On an entirely different principle is the Alnor velometer which was introduced in this country only a few months ago. It gives a direct and immediate reading of the velocity in feet per minute. It can also be used for many other determinations relating to air supply.

The katathermometer, to be referred to later, while most commonly employed for another determination, can also be used for measuring air-flow and is a very sensitive instrument for this purpose.

The amount of air which should be supplied is 2,000 to 3,000 cubic feet per man per hour, but this is only one factor, and it is becoming more and more recognized that adequate floor space is at least equally important.

Temperature and humidity.—The next question is the maintenance of comfort and a feeling of well-being. This requires the conditions to be such that they do not restrict the loss of heat, which must be occurring continuously from the individual, if discomfort and, in extreme cases, heat exhaustion, and in still more extreme cases, heat stroke, are not to result.

In temperate climates the loss of body heat is by radiation and convection, and in hot climates this is enormously reinforced by evaporation of perspiration. The first requisite, then, is that the air should have a moderate temperature and humidity. These are determined by recording the wet and dry bulb temperatures, and thence the relative humidity is ascertained by referring these to tables. For continuous records thermo-hygrographs are employed.

In temperate climates the dry-bulb temperature is the chief interest, but in hot climates the wet-bulb temperature is the main concern, for the individual covered with perspiration is in reality a human wet-bulb.

What is to be considered a satisfactory dry-bulb temperature? It is impossible to lay down figures acceptable to everybody, but I think the greatest measure of agreement will be accorded to the following: For hard-work 60-62° F., for sedentary work 62-64° F., and for leisure 64-66° F., with a relative humidity of 70-75 per cent.

Regarding wet-bulb temperatures, the figures promulgated by Haldane as limits are widely quoted: In still air, 88° F. for sedentary work, and 78° F. for hard work; in moving air, 93° F. for sedentary work and 85° F. for hard work. As the result of numerous observations of hot temperature conditions I think that the figures could be placed higher.

It is remarkable what the individual can stand, at least for a short period. Last summer 40 of us were in an air-tight space in which the wet-bulb temperature was 88° F. and the relative humidity 82 per cent., rising in a period of three-quarters of an hour to a wet-bulb temperature of 96.2° F. and a relative humidity of 99 per cent. Such conditions have to be experienced to be understood, conditions in which the more elegant term perspiration becomes wholly inadequate and one's mind is occupied with the all-pervading sweat. Yet none of the personnel exhibited symptoms of distress.

Cooling power.—An examination of the temperature and humidity provides a certain amount of information as to whether the conditions are such as to interfere with the loss of body heat, but there is another factor to be considered. Suppose in this hall we had a high temperature and a high humidity. Everybody would be most uncomfortable. Suppose now electric fans were brought into operation. Immediately there would be a sensation of relief and comfort. Yet the dry-bulb temperature will not have altered, neither will the wet-bulb, and the relative humidity will still be the same. The beneficial effect of air movement is due to this continuously dispersing the envelope of hot humid air surrounding the individual between the skin and his clothes thereby promoting heat loss by evaporation, and by increasing that due to convection. In other words, the cooling power of the air has been increased.

The cooling power is determined by the katathermometer devised by Sir Leonard Hill. The katathermometer record is obtained in terms of heat-loss in millicalories per sq. cm. per second. The indications have been determined empirically, and it has been laid down that the most suitable conditions are those giving a dry kata of 6 and a wet kata of 18. Personally, I think most people would find such conditions chilly, and that more generally applicable standards are 5 and 15 respectively.

In the tropics the dry kata falls so slowly, and may indeed rise, that it is useless and only the wet kata is employed. Under tropical conditions a figure of 10 should be the aim, but 8 can scarcely be regarded as unsatisfactory. A modified katathermometer is available for use in very high temperatures; the figures given refer to the ordinary katathermometer.

Effective temperature.—Apart, then, from the dilution of respiratory impurity in the air, the ventilation conditions will be assessed by the combined effect of dry and wet bulb temperatures, the relative humidity, and the air movement.

In America this combined effect has been termed "effective temperature", and a chart has been prepared from which this can be deduced. An effective temperature of say, 65° F., is the equivalent of air at 65° F., saturated, and motionless.

As the result of a very large number of empirical observations the American investigators have decided the conditions which the majority of their countrymen consider comfortable, and a comfort zone has been incorporated in the chart. But for very good reasons American ideas of comfort in ventilation are quite different from our own, so the chart is not applicable to conditions in this country.

Air-Conditioning in Factories

By C. W. PRICE

(H.M. Engineering Inspector of Factories)

IN any general discussion on air-conditioning of occupied rooms or chambers, applied solely for the benefit of the health and comfort of the occupants, it is essential to consider factory workrooms in a class apart, and this for several reasons. As a Home Office official I can, perhaps, assist this discussion best by dealing with some of these reasons, and by pointing out certain difficulties which must hinder the adoption of complete air-conditioning, as we now understand the term, for improving conditions for factory workers.

The outstanding feature which characterizes the industrial field in this connexion is the infinite variety of conditions in various industries. One ship's cabin is much like another, theatres compare with theatres, schools with schools, but how can factories be compared? Consider them from the standpoint of the Factory Acts. Besides the general run of factory premises—for instance, printing works, bookbinding works, tobacco factories, and works for the production of clothing, boots and shoes, and small wares and goods of all kinds—the term “factory” covers flour mills, textile works, cement works, potteries, paint and colour works, dye works, gas works, electrical stations, and many more which present unique conditions.

While there is no doubt that a proportion of these factories could be air-conditioned, if that were regarded as necessary, I think it is obvious that in a large number of factories or parts of factories, complete air-conditioning will not be adopted. Nor will it be recognized as within the realm of practical politics.

Even within the confines of a single workroom, the needs of workers may differ greatly. Some may be at furnaces or otherwise exposed to considerable heat, others may be near windows which produce considerable cooling. The workers may be crowded in some parts while comfortably separated in others. Some may be seated, engaged on quiet easy tasks, while others may be working strenuously. In such circumstances, the problem of air-conditioning, in its physical aspects, is, indeed, a difficult one. In this connexion the advent of the large single story, partitionless factory, has not been an unmixed blessing.

There is, on the other hand, a large range of premises to which complete air-conditioning could be applied with as little difficulty as to non-industrial premises—offices, cinemas, and so on. Such air-conditioning, adopted with the sole object of controlling atmospheric conditions in the workrooms for the well-being of workers, has not yet taken root in Great Britain. A considerable number of air-conditioning plants, embodying efficient filtration arrangements for cleaning the air supply, are in use in our factories. They have been provided, however, to secure improved results in production—for example, to ensure a clean product, or to control temperature and humidity for drying or cooling purposes. These plants have found their way into various branches of the food industry, breweries, photographic works—and even the steel industry—but, so far as present information goes, they cannot, as a general rule, be claimed as means for rendering the atmospheric conditions for workers ideal. It is, indeed, tolerably certain that, apart from the cleaning of the air supply, the introduction of these aids to scientific production may, in some cases, render conditions of temperature or humidity less satisfactory for the workers.

A large number of plants which partially condition the air supply have been installed for the purpose of benefiting the workers. Such plants include the plenum ventilating installations, for supplying warmed air in cold weather. They are in some cases combined with air-filtering arrangements. They are found in a very wide range of industries, particularly those in which sedentary or other light work is

carried on. A number of plenum installations are also in use for supplying cool air to furnace workers, or others subject to high temperature.

In addition, many air-exhausting plants are in service for extracting deleterious products of manufacturing processes. These products may be in the form of dust, fume, vapour, or gas. The extraction installations may be responsible for the whole of the ventilation of the rooms concerned, since the air extracted must be steadily replaced. The air may be renewed by natural inflow, without temperature conditioning, but where a considerable rate of air extraction is necessary, a warmed "plenum" supply should be provided to regulate the temperature, or the air should be passed through heaters at the inlets. Unless the air supply is thus directly heated, conditions for the workers in cold weather may be very uncomfortable, or even harmful, ordinary heating equipment being inadequate to maintain a reasonable temperature. Because of this discomfort, the workers may block up the extraction ducts, or in some other way render the fume or dust extraction arrangements ineffective, a most unfortunate consequence of a too-restricted air-conditioning. Happily, the practice of heating the air supply is extending, but there are many works where the provision of efficient fume or dust extraction arrangements is attended at times by discomfort for the workers, because such heating is lacking.

The regulation of humidity, in this country, with the object of setting up what some might consider ideal conditions for the workers in this particular respect, has so far not been adopted in the ordinary factory. Thus there is nothing comparable with the more complete air-conditioning practice of the United States or of Canada, where humidity, as well as temperature, is duly regulated. This is explained by the fact that external temperature and humidity variations in Great Britain are, normally, much more restricted. In consequence, regulation of indoor humidity in Great Britain seldom becomes necessary for dealing with large variations in the external atmosphere. It is true to say that if ordinary factories are adequately ventilated, as the law requires, the problem of humidity is and will continue to be regarded as of little significance.

The large air space which must be provided for factory workers is a factor also to be borne in mind in assessing industrial atmospheric conditions.

The urge on the employers to comply with the provisions of the Factory Acts has undoubtedly contributed to the measure of advance, in factories, towards the partial air-conditioning, to which I have referred. This legal urge has, in fact, been the principal incentive. A short consideration of the requirements of the present law, and of the proposals introduced in the Bill now before Parliament, may perhaps not be out of place in this contribution to the present discussion.

Certain legal provisions, aimed at controlling atmospheric conditions, apply generally to workrooms in all industries, the various atmospheric factors subject to such control being regulated independently of one another. Be it noted that there is no requirement dealing with the cleanliness, temperature, or humidity of the air supply, or with the relative or the absolute humidity of the internal atmosphere. There must, however, be sufficient ventilation, a reasonable temperature, having regard to the kind of work being done, and adequate removal of deleterious products attending manufacturing operations, to prevent such being emitted into the atmosphere of the workrooms. There are no specific standards of general application, for controlling ventilation and temperature. Such standards as are enforceable by supplementary provisions in Codes of Regulations, which regulations are moreover applicable only to particular industries, cannot be said to do more than prevent undue discomfort. Such indeed is their aim, rather than the creation of an ideal environment. The control of artificial humidity, by the Cotton Cloth Factory Regulations, illustrates this.

The Factories Bill, now under discussion, contains both modified and new provisions for the regulation of atmospheric conditions in the generality of workrooms.

If these provisions become law, they will assist in bringing about somewhat more efficient air-conditioning in many workrooms. For one thing, specific regulation of temperature would apply over a wide field by the proposed imposition, for certain sedentary work, of a minimum temperature, 60° F., after the first hour.

It is also proposed to require the extraction, where practicable, of any dust whatsoever, evolved in a manufacturing process, if produced in substantial quantity. Present dust removal provisions are limited to harmful dusts. Use of many more dust-extracting appliances can, therefore, be anticipated and, with their introduction, higher standards of ventilation, in the sense of air change, will be attained in the workrooms concerned.

The minimum air space per worker would be raised to 400 cubic feet.

Legal requirements, of themselves, may be regarded as having played but a moderate part in advancing, in industrial premises, the full ideals of the modern air-conditioner. The same will probably be true of their effect in the immediate future. Even so, as higher standards of compliance with legal requirements are secured, and as the requirements themselves are developed, the realization of those ideals will be brought nearer. The Factory Department, whose function it is to enforce the law, has thus assisted towards that eventual realization of ideal temperatures and ventilation standards in workrooms, to which we confidently look forward. In not a few factories advance has already been very far-reaching, not only in workrooms presenting straightforward heating and ventilating problems, but even in workrooms where peculiar difficulties had to be overcome. Such good conditions may be found where dangerous processes are carried on. This has come about because employers have been helpful, and have agreed to the necessary provision for very high standards of ventilation, while not neglecting temperature requirements. With the advent of such efficient arrangements the employers, managers, and workers inevitably begin to speak of the healthy conditions thereby attained. In addition to the two factors, temperature and rate of air change, attention has also been directed to the rates of air movement at working positions and, where of importance, the effects of radiation of heat to or from the individual; radiation is not an "air-conditioning" factor, but one nevertheless to be taken account of in equivalent temperature evaluation, with which we must now become familiar.

In recent years the guidance regarding all these factors, available from the results of the research carried on by the Industrial Health Research Board of the Medical Research Council, has been of great value to the Department, and also to others concerned with ventilating and heating problems in our factories. The recent compendious report—"The Warmth Factor in Comfort at Work"—has notably increased our indebtedness to the Board. Further assistance may also be anticipated from the research now being directed by the Joint Technical Committee for Heating and Ventilation set up by the Council and the Department of Scientific and Industrial Research. I might mention here that quite soon after the opening of the Home Office Industrial Museum, it was decided to provide there an air-conditioning building. This section of the Museum has been of considerable service. Demonstrations are constantly being given there to illustrate the physiological effects of adverse conditions, and air-conditioning methods which may be adopted to remedy them.

The question naturally arises: "To what extent in factories should complete air-conditioning be adopted or recommended?" An attempt has been made to show that in many factories or parts of factories, such an air-conditioning will never be required. As regards workrooms where it might seemingly be adopted with advantage, it is doubtful whether regulation of humidity, as in complete conditioning, is, in general, necessary.

Filtration or cleaning of the air supply may be very desirable in certain cases—for basement and ground-floor workrooms in urban areas, for example; beyond this it does not seem possible to go at present. The moving-out of factories to trading

estates, in more open localities, may be welcomed as achieving the desired result, without the necessity for such treatment of the air.

For the further improvement of factory atmospheric environments, it would seem that the factors likely to require close attention in the future are those with which we have been mainly concerned in the past, and to which reference has been made.

In large numbers of workrooms, improved ventilation is necessary, particularly so in those large rooms which at present lack ventilating fans, but which undoubtedly need them. With better ventilation there must still be due regard to temperature, and the rates of air movement at both foot and head levels. Such a programme would of necessity involve industry in an increased expenditure for fans and for enlarged heating equipment.

Air-Purification and Allergic Conditions

By E. M. FRAENKEL, D.M.

Air-conditioning and air-purification for the use of allergic patients are different in purpose from the usual air-conditioning and the methods used are, therefore, also different. Minute traces of certain substances that may be either contained in the rooms or may come from outside may cause the onset of an allergic condition in a patient. The aim of air-purification in such cases is to afford as complete protection as possible from the allergen in question. These may be climatic and of outdoor origin, as is the case with grass pollen, causing hay fever, or with the "climatic miasms" said by Storm van Leeuwen (1925) to be a frequent cause of asthma. Most of them, however, are impurities which are present or are formed indoors, and these include the material from bedding—such as horsehair or feathers—clothing, dust, and moulds. It has recently been shown that the kapok in mattresses, which was considered to be innocuous when fresh and clean, became a dangerous allergen towards certain patients after it had been in use for some time, during which the action of moulds had caused the formation of breakdown products.

It is for these reasons important that certain points should be taken into consideration in the construction of rooms and in the provision of the contents of these rooms. The walls, floor, and ceiling should be constructed of washable material without any cracks. Special materials such as "eternit" (an asbestos product) have been devised for this purpose. All corners should be round in order to avoid the accumulation of dust. Furniture should be of simple design and constructed of washable material. All the other contents of the room should be of suitable clean material, and an allergic patient should enter the room wearing special clothing.

A number of different ways for making use of air-purification for the benefit of allergic patients have been devised, chiefly on the Continent and in the United States, but this type of treatment has not aroused a great deal of interest in this country. I feel, however, that the method has a wider scope than its application solely to the treatment of allergic patients, as it is possible that ordinary air-conditioning could use a few points from the experiences gained in the treatment of allergic patients. For instance, frequent so-called colds, bronchitis, rhinitis, &c., are, especially when unaccompanied by a rise in temperature, in my opinion and experience more often due to an allergic irritation than to a real infection as is supposed by our scientific superstition. It might therefore be useful if the construction of air-conditioned rooms in general followed some of the principles outlined above.

The various systems designed for air-purification for the use of allergic cases include methods in which the air is cleaned by the freezing of the micro-droplets of water therein, by washing or by electrostatic and other types of air-purification.

The first method of filtration was recommended in 1924 by Storm van Leeuwen, who used two types of air-purification. In the more efficient of these two methods the air is sucked from the top of a shaft 30 metres high and is then subjected to a temperature of -5°C . and reheated. In the second method, which is used for house allergens, the air is filtered through cloth after being introduced from outside. The whole method would possibly be suitable for a small village in Holland but is useless in large towns and industrial areas where the impurities rise to a much greater height than the top of the air-shaft. The former method removes all material present in the form of micro-droplets and up to about 95 per cent. of the fine particles, together with such gases as are dissolved in the micro-droplets of moisture.

Another device recommended by Küster (1928) is the so-called "Wetterfertiger"; in this apparatus the air is cooled to a temperature of 13°C . and washed with water. The temperature is then raised to 21°C . and the humidity adjusted to 65%, the air being distributed by means of an anemostat. A similar method was designed by S. S. and C. S. Leopold (1925), working in the United States. They caused the air to be forced through a water spray in order to render it allergen-free. M. B. Cohen (1927) filtered the air through wool and cotton cloth by means of a fan. This removed 99 per cent. of the pollen and other material with a diameter down to 10μ . Peshkin and Isobel Beck (1930) constructed a filter screen with a number of layers of cellulose, while Rappaport, Nelson, and Walker (1932) used a combination of cellulose filters and "eastern cloth," a woven material made for the purpose of air-purification. L. N. Gay, W. T. Vaughan, and L. E. Cooley (1933) recommended the use of air-conditioning units. The latest advance in air-cleaning is the introduction of the electrostatic cleaner by L. H. Crip and M. A. Green (1936) which, they claim, removes 100 per cent. of the pollen and dust but no gases and vapours. They have found that it is better than mechanical filtration through glass wool, and it has an additional advantage in that it can be operated easily and does not need any replacement.

My own device was produced in 1927 in collaboration with Levy and the engineers of a German manufacturer of gas masks. It was devised in an endeavour to replace the costly cubicles essential to the method of Storm van Leeuwen, with a type of gas mask, working in conjunction with a ventilating fan. The filters are of the same type as used in the ordinary gas mask containing active charcoal and silica gel. There are various layers of porous granular materials, the size of the granules being 1 to 2μ , and the size of the particles retained being as small as $1 \times 10^{-6}\text{ cm}$. Another layer, containing filtration fibres, is able to retain colloidal particles of the same size. After experiments with odiferous gases had been carried out it was shown that the filter was impermeable to pyridine, capronic acid, scatol, tobacco smoke, ammonia, chlorine, and phosgene. Atomization of *B. prodigiosus* and *B. coli* showed that the filter was able to retain 97 per cent. of these organisms. We found that a filter which had been in continuous use for four months retained half of the active material without contamination. In normal use 30 litres of air are drawn through the filter each minute, but this quantity is capable of regulation. The filtered air is inhaled by the patient through a mask fitted with an exhalation valve and goggles, the whole of which can be sterilized in steam. The apparatus can be operated from any domestic electricity supply.

The same principle has been applied to a sleeping-bag which is closed by a zip fastener and to a cubicle similar to that of Storm van Leeuwen, its size being $2 \times 2 \times 2.6$ metres with an air intake of 68.3 cubic metres per hour compared with an inhalation requirement of 10 to 20 litres per minute. (The air is changed six times each hour.) The capacities of the filters for the sleeping-bag and cubicle are different, being in accordance with the space to be dealt with. A combination of the cubicle and the masks and sleeping bags with a high-pressure air supply has been devised in the Charité and other clinics for the treatment of in- and out-patients. In the same way a filter and ventilating fan have been used to provide a whole room or even several

rooms of a building with allergen-free air and, more recently, some of the German spas, e.g. Reichenhall and Ems—specializing in asthma treatment—have used the method of air filtration to render their “pneumatic chambers” (for hypo- and hyper-pressure) free from allergens.

The filtration apparatuses have the same advantages as the electrostatic type in that they do not influence the temperature or humidity of the air if it be taken from an adjacent room, and as the motor is away from the cubicle there is no irritating noise. They have the disadvantage that the filters have to be replaced from time to time, but they are better than the electrostatic apparatus in that they remove gases and vapours.

The latter point is of importance from several points of view. The filtration apparatus can be used as it stands as a protection from allergens, even from those which are, in my opinion, either volatile (epidermal) or dissolved in the micro-droplets present in the atmosphere. Apart from this, noxious gases, such as sulphur dioxide, are removed. These gases, present in the atmosphere of industrial areas, are a source of possible irritation to the mucous membrane of the upper respiratory tract, which is in this way made more sensitive to surrounding allergens. Thirdly, this apparatus, which in time of peace is used for protection from allergens, would provide in time of war an effective protection against poisonous gases. For this reason it is especially suitable for use in hospitals and private houses where there are no specially built gas shelters.

BIBLIOGRAPHY

- BATTA, G., FIRKET, J., and LECLERE E., (1933), “Les problèmes de pollution de l'atmosphère”, Masson et Cie, Paris.
 COHEN, M. B. (1927), *J. Lab. and Clin. Med.*, **13**, 59; 1928, **13**, 963.
 CRISP, L. H., and GREEN, M. A. (1936), *J. Allergy*, **7**, 120.
 FABER and KELL (1936), “Heating and Air Conditioning of Buildings”, Architectural Press, Ltd., London.
 FRAENKEL, ERNST (1930), *Gesundheits Ingenieur*, **53**, 755; (1934), *Schweiz. Med. Wchnschr.*, **64**, 1193; (1937), *Brit. M. J.* (i), 438.
 Id. and LEVY (1927), *Klin. Wchnschr.* **61**, 831; (1928), **7ii**, 2292.
 GAY, L. N. (1933), *J. A. M. A.*, **100**, 1382.
 HANSEN, ROST, and DEKKER, (1930), “Praktikum der Allergischen Krankheiten”, Montana Verlag, Horw-Luzern.
 KESTER, E. (1928), *Ztschr. f. phys. Therap.*, **35**, 301.
 LEOPOLD, S. S. and C. S. (1925), *J. A. M. A.*, **84**, 731.
 NELSON, T., RAPPAPORT, and WALKER (1932), *J. A. M. A.*, **98**, 1861; (1933), **100**, 1385.
 PESKIN, M., and BECK I. (1930), *J. Lab. and Clin. Med.*, **15**, 643.
 STORM VAN LEEUWEN, W., “Allergic Diseases”, Lippincott, Philadelphia, 1925; Springer, Berlin, 1926.
 VAUGHAN, W. T., and COOLEY, L. E. (1933), *J. Allergy*, **5**, 37.

The Chairman pointed out the importance of ventilation and air-conditioning in the Royal Navy. A ship might have to serve one month in the Arctic circle and the next on the equator. The Navy had chiefly to depend on a rapid change of air by mechanical ventilation and warming the incoming air in cold weather. There was never enough cubic space to allow of anything like the minimum space standards usually employed ashore. It should be realized that there was a very wide range of air-conditions, temperature, humidity, and air movement to which the majority of men could comfortably adapt themselves. A minority of individuals, owing to sweating deficiency, or some physiological or psychological defect, could only adapt themselves to a much smaller range of air-conditions; such men were always uncomfortable in the tropics.

He congratulated Dr. Fraenkel on his ingenious “allergen” filter. He realized that a patient in filtered air could be kept free from allergic symptoms, but would like to know if cases of allergy could be permanently cured by this technique.

Dr. V. F. Soothill said that he had had to give the question of air-conditioning some consideration in connexion with the Shops Act and, acting on certain advice, he had adopted a standard of 0.14 per cent. of CO₂ as the maximum permissible.

Sir Weldon Dalrymple-Champneys drew attention to the fact that a psychological factor as well as a physiological one was concerned in the response of an individual to certain conditions of temperature, moisture, &c. He had noticed this particularly under tropical conditions, in tropical forests, in the cabins of ships in the tropics when rough weather or heavy rain necessitated the closing of the port-holes, in deep dugouts in the War, &c. Under these conditions certain individuals felt an oppression which reacted upon their physical condition but was, he was convinced, in part psychological. Sir Weldon also drew attention to a similar effect produced by "stuffiness" in rooms, which was now known to be due, not to a high concentration of carbon dioxide, as was formerly supposed, but to certain odours which were produced under crowded conditions with inefficient ventilation.

Dr. E. Fraenkel (in reply): These types of filtration are of use only in those cases in which air-borne allergens play a rôle. They neither substitute symptomatic treatment with drugs such as adrenalin, nor replace causative treatment such as desensitization or any other treatment which has as its object the raising of the threshold and resistance towards the allergens either locally or generally. They are, however, an additional method which can be used in :—

(1) *Diagnosis*.—(a) To define the entrance of the allergen (conjunctivæ, nose, mouth, or skin). (b) For the differentiation of allergic from psychogenic factors as was shown in the film. (c) For a rough analysis of the types of allergens by the use of filters of varying permeability.

(2) *Prophylaxis*.—In certain trades or professions during work (millers, bakers, furriers, farmers, and laboratory workers); against climatic factors such as dust "miasms" or pollen or against house allergens (moulds, feathers, and house dust) while the patient is asleep.

(3) *Treatment*.—The patient may be protected, and attacks prevented at the time of the protection, if the threshold towards the allergen is very low, and the resistance of the patient near to nil. In other cases, in which the threshold of the "shock cycle" is higher, protection for part of the day or night may be sufficient to prevent the onset of the attack for the whole day.

(4) *Desensitization*.—In the treatment of suitable cases due to air-borne allergens : (a) For beginning a course of desensitization treatment by means of injections under allergen-free conditions, in order that unknown quantities of allergens may be prevented from entering the body at the same time as the injected doses. (b) It has been found that protection for part of the day over a period of some weeks gives an after-effect resembling desensitization; this being due, probably, to the intake of a dose of allergens too small to cause an attack but large enough to act as a physiological form of desensitization.

Finally, we have observed cases in an "asthmatic state" in which ordinary treatment, even under hospital conditions, with frequent injections of adrenalin, did not overcome the condition but which were greatly improved after two or three days' protection in a cubicle, even without the use of such drugs as adrenalin.

Regarding the question of the failure of the electric current during the use of the mask or sleeping-bag during the night, I may emphasize the point that the use of the ventilating fan is actually unnecessary and that it is installed for psychological reasons only. The pressure required for the use of the filter is in fact only equivalent to 5 mm. Hg, a pressure that can easily be overcome by the patient.

Secondly, in the case of the sleeping-bag, the zip fastener is not, in fact, air-tight, and the external air is only excluded by the hyper-pressure due to the fan. Thirdly, the bag may be opened from the inside and a bell is provided, these precautions being a purely psychological requirement.

—
INDEX
—

PROCEEDINGS OF THE ROYAL SOCIETY OF MEDICINE, VOL. XXX, 1936-37.



INDEX

VOL. XXX, 1936-37.

Note.—In this volume two series of numbers are used for pagination, one being the sectional page number and the other the volume page number. The latter only is used in the Index. An asterisk (*) is an indication that German and French abstracts are given of those particular papers.

- Abducens** palsy following spinal anæsthesia, 1007
- Abortion**, criminal, intramural abscess of uterus following, 563
- Acne** conglobata? case of, 1338
- Acrosclerosis** and muscular wasting, poikiloderma with, 1334
- Actinomycosis** of lung, 876
- Active** service, fitness for, effect of aural conditions on, discussion on, 1523
- Adams, A. W.**—Renal pelvic epithelioma with massive calculi and no infection, 1075
Three renal tumours successfully removed from female children aged 3 months, 4½ years, and 14 years respectively, 449
- Adams, Stirk.**—Discussion on otitis media in early childhood, 1308
- Addison's disease**, ? case of, 1058
- Adeno-carcinoma** of kidney, five cases of, 463
- Adenoma** of bronchus (F. J. S. Gower), 673
sebaceum (Pringle's disease) with associated tumours of the nail-beds of the toes, 24
- Adenomyoma** malignum, case of, 563
- Air-conditioning**, carbon dioxide as an index of respiratory impurity, 1541
cooling power, 1543
effective temperature, 1543
measurement of air-supply, 1542
oxygen determination in, 1542
temperature and humidity, 1542
(ventilation conditions and their investigation), discussion on, 1541
in factories (C. W. Price), 1544
- Air-purification** and allergic conditions (E. M. Fraenkel), 1547
- Air-raid** precautions, with special reference to their medical aspects (H. S. Blackmore), 469
- Alimentary** tract, influence of displacements of adjacent organs and of tumours on, 1387
some of the less common lesions of, and special methods of investigation, and the influence of adjacent organs, discussion on, 1371
- Allen, H. W.**—Symmetrical follicular nævus, 370
- Allergic** conditions, air purification and (E. M. Fraenkel), 1547
- *Alston, J. M., and Brown, H. C.**—The epidemiology of Weil's disease, 741
- Alvaro, M. E.**—Transitory tremulous lens, 945
- Amentia**; familial cerebellar diplegia and retinitis pigmentosa, 849
- Anæmia**, aplastic, purpura and, 727
febrile, of obscure origin, 403
hypochromic, congenital heart disease, and peculiar facies, case of, 1189
- *Anæsthesia**, dental, vinyl anæsthesia for (V. Goldman), 891
in U.S.A. and Canada, impressions of, discussion, 937
spinal, neurological sequelæ of, discussion on, 1007
- Anæsthetic** atmospheres, carbon dioxide absorption from (R. M. Waters), 11
- Anæsthetics** for nose and throat operations, choice and technique of, discussion on, 923
- Anæsthetist**, the ideal structure of an operating theatre from the point of view of an (G. Edwards), 331
- Analgesia** during labour, self-induction of, new type of nitrous-oxide machine for (J. Chassar Moir), 1281
- Anderson, R. G., and Weber F. Parkes.**—A subcutaneous glomus tumour (Masson) in the little finger: clinical account, 196
- Aneurysm**, aortic, three cases of, 757
cirroid, involving tongue and floor of mouth, 709
intracranial, traumatic, case of, 854
- Angina** pectoris treated by cardio-omentopexy, 762
- Angioma** of rectum, case of, 1221
serpiginosum, case of, 363
- Animal** and human diseases, epidemiology of (Sir F. Hobday), 835
- Animals** and man, purpuric conditions in, discussion on, 715
purpuric conditions in, 723
- Anthrax**, epidemiology of, 837
- Antiseptics**, urinary (including sodium and ammonium mandelate), discussion on, 501
- Aorta**, perforation of, by swallowed foreign body: two specimens, 499
- Aortic aneurysm**, three cases of, 757
- Arabian** gynæcological, obstetrical and genito-urinary practice illustrated from Albucais (M. S. Spink), 663

- Arabic literature**, an early mention of sleeping sickness in (Max Meyerhof), 670
- Arachnoiditis** (C. M. H. Howell), 33
cerebral forms, 37
effects in region of optic chiasma, 39
in the posterior fossa, 33
on cortex cerebri, 40
spinal forms, 35
- Arm**, tonic spasm of, ? effect of encephalitis, 393
- Artery** of retina, central, and its branches, occlusion of, clinical study of fifty-four cases of (J. Minton), 285
- Arthritis**, chronic, case for diagnosis, 710
rheumatoid, vitamin C in relation to, 1045
- Arthrodesis** in young children (M. Forrester-Brown), 432
indications for, 434
technique, 435
- Arthrogram** to show extent of synovial cavity after synovectomy, 1264
- Ascaris lumbricoides** in alimentary tract, 1377
- Ascorbic acid**, parenteral administration of, in treatment of purpura, 720
- Ashworth, H. K.**—Discussion on neurological sequelae of spinal anaesthesia, 1030
- Asphyxia neonatorum**, blood changes in, 1462
influence of drugs administered to mother upon, 1462
newer methods of resuscitation, 1464
Drinker respirator, 1465
inhalators, 1467
intravenous resuscitation, 1469
laryngeal intubation and insufflation, 1468
lungmotors, pulmotors and resuscitators, 1466
older methods of resuscitation, artificial respiration, 1463
mouth-to-mouth insufflation, 1464
resuscitation in, summary of important facts concerning, 1478-1481
the initiation of respiration in (R. A. Wilson, M. A. Torrey, and K. S. Johnson), 1461
- Asphyxiating gases**, effects of, on the respiratory system, discussion on, 1033
- Aural conditions**, effect of, on fitness for active service, discussion on, 1523
medicine, some problems in (S. H. Mygind and D. Dederding), 1485
- Automatism**, post-traumatic, 1081
- Avery, H.**—Chronic arthritis (case for diagnosis), 710
Splenomegaly with lipaemia, 711
and **Sorsby, A.**—Three cases of the Laurence-Moon-Biedl syndrome, 388
- Ayoub, J. E. M.**—? Haemorrhage from vascular growth of orbit, 946
Uveo-parotitis, 947
- Bacharach, A. L.**—Discussion on nutrition and its effects on infectious disease, 1051
- Bailey, Hamilton.**—Ectopia vesicae, treated by implanting ureters into the bowel, 158
Mitral stenosis with congestive heart failure treated by complete thyroidectomy, 157
Paget's disease affecting left femur only, 157
- Ballantyne, A. J.**—Dysostosis cranio-facialis (with report of case), 280
- Bamber, G.**—Discussion on specific treatment of staphylococcal infections, 518
Epidermolysis bullosa dystrophica, 192
Phenolphthalein eruption, 1059
Phlebectasia, 521
Urticaria pigmentosa, 1059
- Banister, J. Bright.**—Discussion on relative values of upper- and lower-segment Caesarean operations, 551
Intra- and extra-uterine pregnancy. Excision of extra-uterine pregnancy in 4th month, together with rudimentary horn of uterus, followed by full-term delivery of intra-uterine pregnancy, 562
- Barber, H. W.**—Changes in the pilosebaceous follicles and sebaceous secretion following herpes zoster, 975
and **Bishop, P. M. F.**—Keratoderma climactericum (Haxthausen) treated with oestrone, 738
- Bargen, J. Arnold.**—The medical management of chronic ulcerative colitis, 351
- Barium-air three-stage enema**, 1381
- Barris, J. D.**—Discussion on spa treatment of pelvic disorders, 1424
- Basal tumour**, ? case of, 391
- Basden, M.**—Carcinoma of vagina complicating a complete procidentia, 1483
- Bateman, D.**—Epi-tuberculosis showing also bone lesions, 711
- Bauwens, Dr.**—Discussion on short-wave therapy, 220
- Bayon, H. P.**—Transmissible splenomegaly of fowls or reticulo-endothelial leucosis ("erythroleucosis"), 377
- B.C.G.**, single and repeated intravenous injections of, lesions produced in organs of rabbit by: preliminary note (J. R. M. Innes), 887
- Bedford, Evan.**—Discussion on course and management of congenital heart disease, 700
- Belinoff, S.**—Simplified oesophagoscopy: oesophagoscopy without anaesthesia, without head-rest, and without assistance, 496
- Bell, A. C.**—Combined intra-uterine and extra-uterine pregnancy, 562
Intramural abscess of uterus following criminal abortion, 563
- Bennett, Izod.**—Discussion on protamine insulinate, 814
- Bentley, F. H.**—Discussion on injuries of peripheral nerves, 874
- Biggam, J.**—? Massive exudative retinitis, 46
- Bilharzial infection**, papillomata of both kidneys, ureters and bladder ducts, 451
- Biliary cirrhosis** with cyanosis and finger-clubbing, 406
- Birth palsy**, 869
- Bishop, P. M. F.**—Discussion on the present position of hormones in obstetrics and gynaecology, 274
and **Barber, H. W.**—Keratoderma climactericum (Haxthausen) treated with oestrone, 738
- Bjorkman, S.**—Bronchspirometry and its clinical application, with a short account of bronchial catheterization, 477

- Blackmore, H. S.**—Air-raid precautions, with special references to their medical aspects, 469
Discussion on effects of asphyxiating gases on the respiratory system, 1033, 1037
- Bladder** contents, expression of, by pressure and massage, after injury to spinal cord, 1236
malignant growth of, transplantation of ureters into pelvic colon with total cystectomy for (based on seven successful cases (B. Ward), 137
treatment of, in spinal injuries in War (Sir J. Thomson-Walker), 1233
- Blegvad, N. Rh.**—Discussion on the problem of early laryngeal tuberculosis, 221
modern views of concussion of the labyrinth, 321
- Blindness**, "post-influenzal," two cases of, 704
- Bloomfield, A.**—Case of primary carcinoma of Fallopian tube, 52
- Bodman, J.**—Discussion on the peripheral circulation in chronic rheumatism, 621
- Bone**, malignant tumours of, discussion on, 781
Paget's disease of, affecting left femur only, case of, 157
shortening for inequality of length in the lower limbs (R. Brooke), 441
- Bone**, tumours in which the first radiographic signus are changes in the cancellous structure, 791
is localized area of osteoporosis, 785
is localized sclerosis, 787
tumours producing no change in, 783
- Bourne, A.**—Discussion on relative values of upper- and lower-segment Cesarean operations, 557
- Bowman's** membrane, hemispherical formations in, 701
- Boyle, H. E. G.**—Discussion on choice and technique of anaesthetics for nose and throat operations, 924
- Boys, L.**—Discussion on spa treatment of pelvic disorders, 1421
- Brachial** plexus, traction lesions of, 869
- Brailsford, James, F.**—Discussion on malignant tumours of bone, 781
- Brain, R. T.**—Fox-Fordyce disease, case of, 1336
Keratosi punctata, 198
? Lichen planus: case for diagnosis, 1060
Mycosis fungoides, 191
Pseudo-xanthoma elasticum, 199
- Brain, W. Russell.**—Discussion on neurological sequelae of spinal anaesthesia, 1024
Megalencephaly, 391
- Brasher, C. W. J.**—Discussion on effects of asphyxiating gases on the respiratory system, 1037
- Breast**, partial amputation of, for early carcinoma, nine cases of, 166
- Brinton, D.**—Bilateral primary optic atrophy from glioma of optic nerves, 855
- Brockman, E. P.**—(1) Skiagram of three cases of protrusio acetabuli. (2) Case for diagnosis, 572
- Brockman's** operation for talipes varus resulting from defective tibial growth, 207
- Bronchial** catheterization, short account of; bronchspirometry and its clinical applications (P. Frenckner and Stig Bjorkman), 477
- Bronchiectasis**, early, chronic sinusitis with, case of, 708
in children, relation of upper respiratory tract infection to (J. H. Ebbs), 1407
in childhood, surgical treatment of, three cases illustrating, 399
pneumonectomy for, four typical cases of, 760
purpura associated with, 23
- Broncho-pulmonary** suppuration, bronchoscopic therapy in: its mechanism and results (A. Soulas), 492
- Bronchoscopsy** in broncho-pulmonary suppuration: its mechanism and results (A. Soulas), 492
- Bronchspirometry** and its clinical application, with a short account of bronchial catheterization (P. Frenckner and Stig Bjorkman), 477
clinical results of, 484
technique of, 480
- Bronchus**, adenoma of (F. J. S. Gower), 673
- Brooke, R.**—Bone shortening for inequality of length in the lower limbs, 441
The effect of removal of the patella for simple transverse fractures on the function of the knee-joint, 203
- *Brown, H. C., and Alston, J. M.**—The epidemiology of Weil's disease, 741
- Brown, J. W.**—Discussion on course and management of congenital heart disease, 698
- Buckley, C. W.**—Discussion on indications for use of radio-active thermal waters in Great Britain, 827
on the peripheral circulation in chronic rheumatism, 620
- Burnell-Jones, H. S.**—Lupus vulgaris of nose under treatment with tuberculin, 26
- Burnford, J.**—Discussion on medical treatment of chronic ulcerative colitis, 361
- Burrell, L. S. T.**—Discussion on the problem of early laryngeal tuberculosis, 230
on treatment of pleural effusions, 848
- Burrows, H. J.**—An operation for the correction of Madelung's deformity and similar conditions, 565
Brockman's operation for talipes varus resulting from defective tibial growth, 207
- Bush, G.**—Influence of adjacent organs and tumours on the alimentary tract, 1387
- Burt, J. Barnes.**—Discussion on indications for use of radio-active thermal waters in Great Britain, 833
on the peripheral circulation in chronic rheumatism, 620
- Butler, T. Harrison.**—Discussion on epithelial growths of conjunctiva and cornea, 1279
- Buxton, St. J. D.**—Discussion on prevention and treatment of ununited fractures, 993
- Cæsarean** operations, upper and lower-segment, relative values of, discussion on, 551
section, lower segment, advantages of, and results, 554, 555
statistics and indications, 553

- Calculus, ureteric, large, 1079**
- Cambrook, J. D.**—Discussion on therapeutic methods of arresting hæmorrhage, 652
- Campbell, S.**—Chronic sinusitis with early bronchiectasis, 708
- and **Hardy, A. J.**—Actinomycosis of lung, 876
- Canada and U.S.A.**—Anæsthesia in, impressions of, 937
- Capener, N.**—Intractable sciatica due to prolapsed intervertebral disc, treated by laminectomy, 1262
- Capillaries in nailbed, condition of, in normal and rheumatic conditions, 616-619**
- Capps, F. W.**—Discussion on orbital cellulitis due to sinus infection and its treatment, 1404
- Carbon dioxide absorption from anæsthetic atmospheres (R. W. Waters), 11**
- advantages, 18, 19
- chemistry, 14
- controlled respiration, 20
- essential factors in application to clinical anæsthesia, 17
- historical aspects, 11
- technique, 18
- as index of respiratory impurity, 1541
- Carcinoma erysipelatodes, case of, 983**
- Carcinoma, seven cases of, showing result of treatment, 934**
- Cardio-omentopexy, angina pectoris treated by, 762**
- Carmichael, E. A.**—Occipital lobectomy, 953
- Carnivora, innervation of periodontal membrane in, 1358**
- Carpus, degeneration of, produced by use of a compressed air-drill, 210**
- Carswell, R.**—Lupus vulgaris of nose under treatment with tuberculin, 26
- Carter, J. A.**—Three cases illustrating surgical treatment of bronchiectasis in childhood, 399
- *Carver, J.**—Observations on genito-urinary tuberculosis, 1429
- Specimen of: (1) Large adenoma of kidney with hæmorrhage into growth. (2) Carcinoma of ureter with hydronephrosis and secondary growths in bladder. (3) Multiple papillomata filling pelvis of kidney, 453
- Cass, E. E.**—Two cases of ocular torticollis, 1264
- Cat, innervation of periodontal membrane in, 1358**
- purpuric conditions in, 725
- Catheter, indwelling or tied-in, use of, in treatment of bladder after injuries to spinal cord, 1238**
- Cattle and sheep, paratuberculosis in (G. W. Dunkin), 83**
- purpuric conditions in, 724
- Cauda equina, lesions of, following spinal anæsthesia, 1008**
- Cawthorne, T.**—Discussion on effect of aural conditions on fitness for active service, 1531
- Cellulitis, orbital, due to sinus infection, and its treatment, discussion on, 1397**
- Cerebellar lobe, left, tumour of, 395**
- Cerebral pathology, diagnosis of, the electro-encephalogram in, 578**
- Cerebral tumour, the: electro-encephalogram in cases of (W. Grey Walter), 579**
- Cerebro-macular degeneration, ? case of, 388**
- Cervix, carcinoma of, complicating procidentia uteri, two cases of, 1343**
- circumscribed polypoid sarcoma of, 49
- Challis, J. H. T.**—Discussion on choice and technique of anæsthetics for nose and throat operations, 929
- Chauffard-Still Syndrome (Feltz's syndrome), 932**
- Chick, H.**—Discussion on nutrition and its effects on infectious disease, 1042
- Childhood, early, otitis media in, discussion on, 1293**
- Children and adolescents, internal derangement of knee in (H. A. T. Fairbank), 427**
- diseases of, relation of the ear, nose and throat to (B. Morgan), 1415
- early bronchiectasis in, relation of upper respiratory tract infection to (J. H. Ebbs), 1407
- normal hearing of, measurement of, 1497
- young, arthrodesis in (M. Forrester-Brown), 432
- Chloasma virginum periorale, ? case of, 1057**
- Choanal atresia, unilateral, in a woman, aged 23, 917**
- Chondro-osteo-dystrophy (Brailsford-Morquio type), case of, 160**
- Choroid, sarcoma of? Retinitis exudativa externa? case of, 948**
- Choroidal growth, ? case of, 947**
- sclerosis, peripapillary, two cases of: a familial group, 286
- Choroiditis, juxtapapillary (Jensen), case of, 948**
- tuberculous or metastatic, case of, 706
- Christie, R. V.**—Discussion on effects of asphyxiating gases on the respiratory system, 1035
- *Circulation, peripheral, in chronic rheumatism (G. D. Kersley), 611**
- Circumflex nerve palsy in subcoracoid dislocations, 864**
- Cirrhosis with jaundice: cholecystgastrostomy, 878**
- Cirsoid aneurysm involving tongue and floor of mouth, 709**
- Cleft palate, case to illustrate a method of stabilizing a denture by means of a gold jacket crown, 1253**
- Cleido-cranial dysostosis, case of, 882**
- Cleminson, F. J.**—Discussion on labyrinthine reactions and their relation to the clinical tests, 914
- Coal-mining, Weil's disease and, 750**
- Cockayne, E. A.**—Gargoylism (chondro-osteodystrophy, hepatosplenomegaly, deafness), in two brothers, 104
- Myositis ossificans progressiva, 162
- Colitis, mucous or mucomembranous, 1215**
- ulcerative, 1215
- chronic, ætiology of, 351
- diagnosis of, 355
- medical management of (J. A. Bargen), 351
- pathology of, 354
- treatment of, 356
- Colon, diseases of, age and sex incidence of, 1212**
- cancer, 1218
- constipation in, 1213
- diverticulosis and diverticulitis, 1216

- Colon**, diseases of, flatulence in, 1213
 general diagnosis in, 1212
 incidence of, 1211
 ptosis in, 1213
 redundancy of sigmoid, 1214
 incidence and treatment of (Sir E. Spriggs), 1211
 volvulus, 1215
 investigation of, special methods of, 1381
 pelvic, transplantation of ureters into, with total cystectomy, for malignant growth of bladder, based on seven successful cases (B. Ward), 137
- Coltart**, W. D.—An early case of dyschondroplasia, 202
- Comparative** medicine and its relation to the study of tropical medicine (P. H. Manson-Bahr), 237
- Complement-fixation** test in diagnosis of paratuberculosis of cattle and sheep, 87
- Concussion**, after-effects of, 1081
 clinical features, 1081
 of labyrinth, modern views of (N. Rh. Blegvad), 321
- Conjunctiva** and cornea, epithelial growths of (E. F. King), 1273
- Conus** medullaris, lesions of, following spinal anaesthesia, 1008
- Copeman**, W. S. C.—Discussion on the peripheral circulation in chronic rheumatism, 622
- Corbett**, R. S.—Discussion on medical treatment of chronic ulcerative colitis, 362
- Cornea** and conjunctiva, epithelial growths of (E. F. King), 1273
- Corneal** dystrophy, three cases of, 389
 ulceration, delayed, following mustard gas burns, 949
- Corsi**, H.—Lichen planus associated with atrophy of nail matrix and hair follicles of scalp, 198
- Cortical** sclerosis, symmetrical, localized, in an infant, 1095
- Cow**, infection of, human infections associated with, 951
- Cowell**, S. J.—Discussion on nutrition and its effects on infectious disease, 1039
- Craniofacial** dysostosis (Crouzon's syndrome), case of, 1187
- Critchley**, M.—Colloid cyst of third ventricle, 850
 Discussion on neurological sequelæ of spinal anaesthesia, 1007
 Paget's disease of skull associated with a pituitary neoplasm, 849
 and Greenfield, J. G.—Jakob's syndrome (senile dementia with Parkinsonism), 1100
- Crohn's** disease, case of, 1375
- Crooke**, A. C.—Three cases of eunuchoidism, 1199
- Crouzon's** syndrome (craniofacial dysostosis), case of, 1187
- Crowe**, H. W.—Discussion on nutrition and its effects on infectious disease, 1051
- Cubitt**, A. W.—Discussion on urinary antiseptics, 508
- Cumberbatch**, E. P.—Discussion on short-wave therapy, 211
- Cumberlidge**, W. I.—Discussion on operative treatment of uncomplicated inguinal hernia, 531
- Cystectomy**, total, with transplantation of ureters into pelvic colon for malignant growth of urinary bladder (based on seven successful cases) (B. Ward), 137
- Cysticercosis**, case of, 577
- Cystoscopy**, value of, in diagnosis of renal tuberculosis, 1437
- Cystotomy**, early or prophylactic, in treatment of bladder after injuries to spinal cord, 1238
- Dalrymple-Champneys**, Sir W.—Discussion on air-conditioning, 1550
 transmission of Brucella infections, 840
 Remarks on snake venom, its source, method of collection and uses, 1453
- Davenport**, C.—Purpuric conditions in animals, 723
- Davidson**, L. S. P.—Discussion on purpuric conditions in man and animals, 715
- Davidson**, M.—Discussion on therapeutic methods of arresting hæmorrhage, 647
- Davies**, J. H. T.—Hæmolympheangioma, 197
- Davies**, T. E.—? Choroidal growth, 947
- Davis**, E. D. D.—Discussion on effect of aural conditions on fitness for active service, 1529
 on orbital cellulitis due to sinus infection and its treatment, 1397
 on physical aspects of tinnitus, 1518
- Deaf** children; ages of incidence of deafness, 1495
 audiograms of, special cases of, 1503
 causes of deafness in, 1496
 hearing and speech in (P. M. T. Kerridge), 1494
 test results with, 1500
 tests used for, 1496
 incidence of, 1494
 proficiency in speech in, 1507
 specific fevers causing the deafness, 1496
- Deafness** after radical mastoid operations, characteristics of, 1486
 after suppurative otitis media, characteristics of, 1487
 in otosclerosis, characteristics of, 1486
 of syphilitic and traumatic origin, characteristics of, 1487
 perception, characteristics of, 1485
- Decompression** chamber, description of, 1002 *et seq.*
- Dederding**, D., and **Mygind**, S. H.—Some problems in aural medicine, 1485
- De Kleijn**, Dr.—Discussion on labyrinthine reactions and their relation to the clinical tests, 914
- Denny-Brown**, D. E.—Mild eunuchoid giantism, 857
- *Dental** anaesthesia, vinyl ether anaesthesia for (V. Goldman), 891
 cyst, large, arising in left maxilla and obstructing the nose, 1252
 (right mandible), 1250
 extraction, acute osteomyelitis and death following, 1241
- Dermatomyositis**, ? artefact, case of, 1337
 case of, 109, 195
- Descemet's** membrane of left cornea, birth rupture of, 390

- ? **Devic's** disease retrobulbar neuritis, case of, 394
- Diabetes**, protamine insulinate in (H. C. Hagedorn), 805
- Diaphragmatic** hernia of traumatic origin in a child, 758
- Diaphyseal** aclasis, case of, 110
- Diet**, raw vegetable, in chronic rheumatic conditions, therapeutic trial of (D. C. Hare), 1
- Diphtheria**, active immunization against, by the combined subcutaneous and intranasal method (C. Jensen), 1117
- Diphtheroid** ulceration, case of, 1059
- Disease**, cause of, milk as a factor in, discussion on, 951
- Dislocations** and fractures, nerve injuries accompanying, 864
- Displacements** of adjacent organs, influence of, on alimentary tract, 1387
- Distichiasis**, familial, two cases of, 390
- Diverticulitis**, 1216
- Diverticulosis**, 1216
- Dix, V. W.**—Grawitz tumour of unusually low malignancy, 459
- Papilloma and intussusception of ureter, 456
- Dobbs, R. H.**—Malrotation of intestines in a child aged 9 months: cured by operation, 404
- Two cases of pyloric stenosis treated with Eumydrine, 1193
- Dodds, E. C.**, Discussion on the present position of hormones in obstetrics and gynaecology, 263
- and **Noble, R. L.**—The action of pituitary extracts on gastric secretion, 815
- Dog**, purpuric conditions in, 725
- Dottridge, F. S.**—Mycosis fungoides, 191
- Dougal, D.**—Discussion on spa treatment of pelvic disorders, 1422
- Doyné, P. G.**—Congruous field defects due to congenital absence of nerve-fibres, 946
- ? Haemorrhage from vascular growth of orbit, 946
- Retinal changes in case of purpura, 946
- Uveo-parotitis, 947
- Drinker** respirator in treatment of asphyxia neonatorum, 1465
- Drugs** administered to mother, influence of, upon asphyxia of the new born, 1462
- Dudley, S. F.**—Discussion on air-conditioning, 1549
- The ecological outlook on epidemiology, 57
- Dukes, C.**—Histological grading of rectal cancer, 371
- Non-malignant tumours of kidney necessitating nephrectomy, 447
- Dunkin, G. W.**—Paratuberculosis in cattle and sheep, 83
- Duodenum**, primary, carcinoma of, 1375
- Dyschondroplasia**, early case of, 202
- Dysostosis** crania-fascialis, with report of case (A. J. Ballantyne), 280
- Ear**, nose and throat, relation of, to the diseases of children (B. Morgan), 1415
- East, Terence.**—Discussion on course and management of congenital heart disease, 696
- East, Terence.**—Three cases of aortic aneurysm, 757
- Two cases of Pick's syndrome, 763
- Ebbs, J. H.**—Discussion on otitis media in early childhood, 1297
- The relation of upper respiratory tract infection to early bronchiectasis in children, 1407
- Ecological** outlook on epidemiology (S. F. Dudley), 57
- Ectopia** vesicae treated by implanting ureters into the bowel, case of, 158.
- Edwards, G.**—The ideal structure of an operating theatre from the point of view of an anaesthetist, 331
- Edwards, H.**—Exomphalos associated with volvulus neonatorum: result six and a half years after operation, 881
- and **Sheldon, W.**—Cirrhosis with jaundice: cholecystgastrostomy, 878
- Congenital recto-sigmoid stricture, 1192
- Edwards, J. T.**—Discussion on nutrition and its effects on infectious disease, 1046
- on purpuric conditions in man and animals, 728
- Ehlers-Danlos** syndrome, cases of, 30, 984
- Eidinow, A.**—Discussion on short-wave therapy, 219
- Elbow**, fractures and dislocations of nerve-lesions in, 866
- Electrical** stimuli, results of, in injuries of peripheral nerves, 871
- Electro-encephalogram** in cases of cerebral tumour (W. Grey Walter), 579
- in the diagnosis of cerebral pathology, 578
- Elkeles, A., Sorsby, A., Goodhart, G. W., and Morris, I. B.**—Experimental staining of retina in life, 1271
- Elkington, J. St. C.**—Medulloblastoma of fourth ventricle with repeated spinal recurrences, 396
- Polioencephalitis hemorrhagica superior, 1096
- Elliot, J. M.**—Pringle's disease (adenoma sebaceum) with associated tumours of the nail-beds of the toes, 24
- Ellis, R. W. B.**—Chondro-osteo-dystrophy (Brailsford-Morquio type), 160
- Craniofacial dysostosis (Crouzon's syndrome), 1187
- Diaphragmatic hernia of traumatic origin in a child, 758
- Diaphyseal aclasis, 110
- Gargoylism (chondro-osteo-dystrophy, corneal opacities, hepato-splenomegaly and mental deficiency), 158
- Internal hydrocephalus following cerebral thrombosis in an infant, 768
- Ellis, V. H.**—Obscure lesion in the tibia, 203
- Ellman, P.**—Discussion on the peripheral circulation in chronic rheumatism, 621
- Embolectomy**, peripheral (V. H. Riddell), 684
- Embleton, D.**—Rhythmical neutropenia with recurrent buccal ulceration, 980
- Enema**, barium air three-stage, 1381
- thorium three-stage, 1382, 1383
- Endothelioma** of tibia (with pathological fracture), 766
- Epidemic** factors, measurement of, 58

- Epidemics**, clinical picture and bacterial type, 65
density and rate of change of population in relation to, 62
malnutrition and, 64
natural active immunization and, 59
parasitic aberrancy and new diseases, 67
mutation as cause of, 66
variation in, 64
- Epidemiologist**, Fracastor as an (E. W. Goodall), 341
- Epidemiology**, ecological outlook on (S. F. Dudley), 57
of animal and human diseases (Sir F. Hobday), 835
- Epidermolysis** bullosa dystrophica, case of, 192
- Epilepsy**, puff-adder venom in treatment of, 1453, 1454
- Epithelial** growths of conjunctiva and cornea (E. F. King), 1273
- Epi-tuberculosis** showing also bone lesions, 711
- Epulis**, fibrous, between 2 & 1, 1249
- Erythrodermia**, leukemic, case of, 192
- Eunuchoid** giantism, mild, case of, 857
- Eunuchoidism**, three cases of, 1199
- Evans**, H.—Discussion on effects of asphyxiating gases on the respiratory system, 1037
- Evans**, P. R.—Biliary cirrhosis with cyanosis and finger-clubbing, 406
Cirrhosis with jaundice: cholecystgastrostomy, 878
Dermatomyositis, 109, 195
Hypoehronic anemia, congenital heart disease, and peculiar facies, 1189
Specimen of congenital genito-urinary abnormalities with suprarenal enlargement, 1190
- Everidge**, J.—Diffuse papillomatosis: removal of kidney, ureter, and part of bladder, 448
Discussion on urinary antiseptics, 514
Primary papillomata of ureter, secondary hydro-nephrosis and transplant deposits in bladder. Removal of kidney and ureter. Recovery, 449
- Eyelid**, upper, left, superficial cicatrizing rodent ulcer of, 1393
- Exomphalos** associated with volvulus neonatorum: result six and a half years after operation, 881
- Face**, chronic sinus of, case of, 1068
- Facial** cleft, secondary unilateral, with excess tooth and bone formation, 79
- Factories**, air-conditioning in (C. W. Price), 1544
- Fairbank**, H. A. T.—Discussion on prevention and treatment of ununited fractures, 990
Internal derangement of knee in children and adolescents, 427
- Fallopian** tube, primary carcinoma of, case of, 52
- Featherstone**, H. W.—Discussion: impressions of anaesthesia in the U.S.A. and Canada, 937
- Feet**, skin of, fungus infection of, clinical note on (J. C. Souter), 1107
- Feilden**, F. E.—Discussion on genito-urinary tuberculosis, 1442
- Felling**, A.—Discussion on neurological sequelae of spinal anaesthesia, 1032
- Felling**, A.—Tonic spasm of arm: ? effect of encephalitis, 393
and **Wright**, A. Dickson.—Spina bifida occulta with nervous symptoms: relieved by operation, 574
- Felty's** syndrome (Chaffard-Still syndrome), 932
- Femur**, head of, necrosis of, following fracture of neck in a child, 210
incomplete fracture of, case of, 201
- Ferguson**, F. R.—Discussion on neurological sequelae of spinal anaesthesia, 1020
- Ferret**, innervation of periodontal membrane in, 1360
- Fibrositis**, treatment of by radio-active thermal waters in Great Britain, 829
- Field-work**, Weil's disease and, 751
- Finzi**, N. S.—Treatment of distant malignant metastases, 779
- Fish**, E. W.—Local and remote sequelae of infection in the parodontal sulcus, 1149
- Fish-cleaning**, Weil's disease and, 752
- Fitzwilliams**, D. C. L.—Nine cases of partial amputation of breast for early carcinoma, 166
Seven cases of carcinoma showing result of treatment, 934
- Flying**, high, respiration in (G. S. Marshall), 995
pressure suit for use in, 1001
uses of decompression chamber, 1002, *et seq.*
- Fœtal** blood, changes in, in asphyxia neonatorum, 1462
- Fœtus** amorphus (anidus) case of, 564
- Foot-and-mouth** disease, epidemiology of, 837
outbreaks in European countries, statistics of, 838
- Forman**, L.—Diphtheroid ulceration, 1059
Discussion on specific treatment of staphylococcal infections, 519
Erythema multiforme type of pemphigus, 369
? Idiopathic trichoclasia, 527
Superficial ulcerating tuberculosis of skin, 369
- Forrester-Brown**, M.—Arthrodesis in young children, 432
- Forster**, H. V.—Discussion on labyrinthine reactions and their relation to the clinical tests, 914
on sinography, 422
- Fowls**, erythroleucosis of, 377
tumour formation and, 381
transmissible splenomegaly (of reticulo-endothelial leucosis "erythroleucosis") (H. P. Bayon), 377
experiments and tests with a Budapest virus, 380
- Fox-Fordyce** disease, case of, 1336
- Fracastor** as an epidemiologist (E. W. Goodall), 341
- Fractures** and dislocations, nerve injuries accompanying, 864
ununited, bone infection in relation to, 988
over-extension in relation to, 988
prevention and treatment of, discussion on, 987
skeletal traction in relation to, 988, 993
- Fraenkel**, E. M.—Air-purification and allergic conditions, 1547

- Frankau, C. H. S.**—Discussion on operative treatment of uncomplicated inguinal hernia, 536
- Franklin, A. White.**—Precocious puberty in girl aged 4 years, 101
- Franklin, S. M.**—Chronic arthritis (case for diagnosis), 710
Splenomegaly with lipaemia, 711
- Frederick, R. C.**—Discussion on air-conditioning (ventilation conditions and their investigation), 1541
- Frenckner, P.**—Bronchspirometry and its clinical application, with a short account of bronchial catheterization, 477
Sinography: a method of radiography in the diagnosis of sinus thrombosis, 413
- Freudenthal, W., and Weber, F. Parker.**—Nodular non-diabetic cutaneous xanthomatosis with hypercholesterolaemia and atypical histological features, 522
- Fripp, A. T.**—Incomplete fracture of femur, 201
- Frontal lobectomy, left, two cases of.** 851
- Fungus infection of the skin of the feet, clinical note on (J. C. Souter),** 1107
- Gabriel, W. B.**—Angioma of rectum, 1221
Meckel's diverticulum causing severe recurrent haemorrhage from the bowel, 1220
- Gage, Courtney.**—Discussion on some of the less common lesions and special methods of investigation of the alimentary tract and the influence of adjacent organs, 1371
- Galbraith, W. W.**—Discussion on the Harris operation and its modifications, 1230
- Gangrene of skin, post-operative, progressive (A. M. Stewart-Wallace),** 681
- Ganglio-neuroblastoma, mediastinal, case of,** 1195
- Gardiner-Hill, H.**—Discussion on the present position of hormones in obstetrics and gynaecology, 266
- Gargoylism (?) (chondro-osteo-dystrophy),** 1070
(chondro-osteo-dystrophy, corneal opacities, hepatosplenomegaly and mental deficiency), case of, 158
(chondro-osteo-dystrophy, hepatosplenomegaly, deafness) in two brothers, 104
- Garland, A.**—Mitral stenosis with congestive heart failure treated by complete thyroidectomy, 157
- Garrod, L. P.**—Discussion on medical treatment of chronic ulcerative colitis, 361
- Gastric secretion, action of pituitary extracts on (E. C. Dodds and R. L. Noble),** 815
- *Gastric ulcer-cancer, frequency of, and the origin of Grawitz tumours of the kidney, the search for truth with special reference to (W. D. Newcomb),** 113
- Gastro-enteritis, incidence of otitis media infection in,** 1302
- General paralysis, a follow-up study, with special reference to malarial therapy (J. E. Nicole and G. J. Harrison),** 623
- Genital tuberculosis, incidence and distribution of,** 1430, 1431
- Genitalia, unusual deformity of, case of,** 1193
- Genito-urinary abnormalities, congenital, with suprarenal enlargement, specimen of,** 1190
obstetrical and genito-urinary practice, Arabian, illustrated from Albucasis (M. S. Spink), 653
- *Genito-urinary tuberculosis, observations on (J. Carver),** 1429
- Gerstman, S. R.**—Cases of: (1) Oxycephaly, showing Apert's syndrome. (2) Two cases of oxycephaly showing Crouzon's syndrome. (3) Ophthalmoplegic migraine, 387
- Giantism, eunuchoid, mild, case of,** 857
- Gibson, A. G.**—Discussion on course and management of congenital heart disease, 699
- Gilliatt, W.**—Discussion on relative values of upper- and lower-segment Caesarean operations, 552
- Girdlestone, G. R.**—Discussion on prevention and treatment of ununited fractures, 991
- Giri, D. V.**—Congenital bilateral ophthalmoplegia externa: a case helped by prisms, 43
- Glanders, epidemiology of,** 836
- Glioma of optic nerves, primary bilateral optic atrophy from,** 855
- Glomus tumour (Masson), subcutaneous, in the little finger. Clinical account,** 196
- Gold casting, research in (W. E. Herbert and A. R. F. Thompson),** 245
- *Goldman, V.**—Vinyl ether for dental anaesthesia, 891
- Goldsmith, W. N.**—Discussion on specific treatment of staphylococcal infections, 519
? Resolving kerion, 521
Scleroderma (or ? scleropanniculomyoderma), 731
- Goodall, E. W.**—Fracastor as an epidemiologist, 341
- Goodhart, G. W., Sorsby, A., Elkeles, A., Morris, I. B.**—Experimental staining of retina in life, 1271
- Gordon, H.**—? Addison's disease, 1058
Benign lymphogranulomatosis with ocular symptoms, 1057
Carcinoma erysepelatoses, 983
Chronic granulomata, 1336
Dermatomyositis: ? artefact, 1337
Fibrous hypertrophy of maxilla, 1252
Lichen planus atrophicus with vesicular onset, 736
? Mycosis fungoides, 367
Necrobiosis lipoidica diabetorum, 527
Pityriasis lichenoides et varioliformis acuta, 191
Scleredema adultorum (Buschke), 983
Scleroderma, 982
- Gordon, M.**—Discussion on aetiology and diagnosis of lymphadenoma, 541
- Gottlieb, B.**—Cysticercosis, 577
- Gould, C. A., and Spear, B. E.**—Mechanical tabulation of hospital records, 633
- Gout, treatment of, by radio-active thermal waters in Great Britain,** 829
- Gowar, F. J. Sambrook.**—Adenoma of bronchus, 673
- Graham, G.**—Discussion on protamine insulinate, 814
on short wave therapy, 220

- Graham, G.**—Discussion on therapeutic methods of arresting hemorrhage, 652
- ***Graham, J. Wallace.**—The toxicity of sterile filtrate from parodontal pockets, 1165
- Granulomata**, chronic, case of, 1336
- Granulosis rubra nasi**, case of, 1054
- Grawitz** tumour of unusually low malignancy, 459
- ***Grawitz** tumours of the kidney, origin of, and the frequency of gastric ulcer-cancer; the search for truth with special reference to (W. D. Newcomb), 113
- Gray, A. M. H.**—Two cases of tuberculide, 735
- Gray, Delisle.**—Discussion on operative treatment of uncomplicated inguinal hernia, 537
- Green-Armytage, V. B.**—Discussion on relative values of upper- and lower-segment Cesarean operations, 557
- Metrochylorrhœa**, 50
- Greenfield, J. G., and Critchley, M.**—Jakob's syndrome (senile dementia with Parkinsonism), 1100
- Griffith, A. D.**—Discussion on epithelial growths of the conjunctiva and cornea, 1280
- Guthrie, D.**—Discussion on effect of aural conditions on fitness for active service, 1538
- on function of the labyrinth, 610
- on otitis media in early childhood, 1316
- on relation of ear, nose and throat to the diseases of children, 1417
- on sinography, 422
- Guttmann, E.**—Discussion on mental disorder following heat injuries, 1093
- Gynæcological**, obstetrical and genito-urinary practice, Arabian, illustrated from Albu-casis (M. S. Spink), 653
- Hæmatomyelia**, spontaneous, report of two cases: one in association with an intramedullary angioma, and the other in association with syphilis, 1101
- Hæmolymphangelioma**, case of, 197
- Hæmophilia**, snake-venom in treatment of, 1454
- Hæmorrhage**, therapeutic methods of arresting, discussion on, 645
- Hagedorn, H. C.**—Protamine insulinate, 805
- Hallpike, C. S.**—Discussion on function of the labyrinth, 609
- on labyrinthine reactions and their relation to the clinical tests, 913
- on some problems of aural medicine, 1492
- Handley, W. Sampson.**—Discussion on value of pre- and post-operative irradiation in malignant disease, 1173
- Hankey, G. T.**—Two cases of osteomyelitis of mandible, 1244
- Hannay, J. W.**—Acholic familial jaundice in the third (? fourth) generation of manifestation of the disease, 1073
- Hardwick, C.**—Undulant fever, 880
- Werdnig-Hoffmann** paralysis in the elder of twins, 1071
- Hardy, A. J., and Campbell, S.**—Actinomycosis of lung, 876
- Hardy, E. A.**—Cleft palate, 1253
- Hare, D. C.**—Discussion on therapeutic methods of arresting hemorrhage, 651
- Hare, D. C.**—Therapeutic trial of raw vegetable diet in chronic rheumatic conditions, 1
- Hare, J.**—Discussion on effect of aural conditions on fitness for active service, 1523
- Harris, L.**—Discussion on nutrition and its effects on infectious disease, 1044
- Harris, W.**—? Basal tumour, 391
- Discussion on neurological sequelæ of spinal anaesthesia, 1031
- Tabes dorsalis** with bilateral trigeminal neuralgia, 573
- Harris** operation and its modifications (C. Morson), 1223
- Harrison, G. J., and Nicole, J. E.**—A follow-up study of general paralysis with special reference to malarial therapy, 623
- Harrison, W. J.**—Discussion on effect of aural conditions on fitness for active service, 1536
- Hart, F. D.**—Febrile anæmia of obscure origin, 403
- Mediastinal ganglio-neuroblastoma**, 1195
- Hasler, J. K.**—Discussion on neurological sequelæ of spinal anaesthesia, 1012
- Headache** following spinal anaesthesia, 1007
- Head injury**, mental disorder following (C. P. Symonds), 1081
- Heald, C. B.**—Discussion on short-wave therapy, 216
- Hearing** and speech in deaf children (P. M. T. Kerridge), 1494
- hard, non-suppurative, characteristics of, 1487
- Heart** disease, congenital, course and management of, discussion on, 633
- rhabdomyomata** in, tuberosc sclerosis with: pathological specimens, 1063
- Heckford, F.**—Delayed corneal ulceration following mustard gas burns, 949
- Heggs, G. B. Mitchell.**—Cutaneous xanthomatosis, associated with established diabetes mellitus, 526
- and **Jacobsohn, F.**—Poikiloderma with parapsoriatic spots treated with thorium X, 367
- Henry, A. K.**—Discussion on operative treatment of uncomplicated inguinal hernia, 534
- Hepatomegaly**, ? cause, case of, 1069
- Hepato-splenomegaly**: ? idiopathic cirrhosis, 409
- Herbert, W. E. and Thompson, A. R. F.**—Research in gold casting, 245
- Herd-immunity**, premuniton in relation to, 61
- Heredity** in neurosis, observations on (R. G. McInnes), 895
- Hermitage, K.**—Malrotation of intestines in child aged 9 months: cured by operation, 404
- Hernia**, diaphragmatic, of traumatic origin, in a child, 758
- inguinal, uncomplicated, operative treatment of, discussion on, 529
- retroperitoneal, 1374
- Herpes** zoster, changes in pilosebaceous follicles and sebaceous secretion following, 975
- Hill, L. C.**—Discussion on indications for use of radio-active thermal waters in Great Britain, 834
- on the peripheral circulation in chronic rheumatism, 622

- Hill, Sir Leonard.**—Discussion on short-wave therapy, 218
- Hip, right, osteo-arthritis of, treated with an extra-articular bone graft. Osteo-arthritis of the right knee, treated with auto-fat injection, 757**
- Hirschsprung's disease, action of bran in treatment of, further report on case shown December 13, 1935, 107**
- Hypernephroma.** See Grawitz tumours.
- Hobday, Sir Frederick.**—Epidemiology of animal and human diseases, 835
- Hobhouse, N.**—Diffuse sclerosis, 931
- Hodgson, Graham.**—Discussion on sinography, 422
- Holfelder, Hans.**—The management of advanced malignancies, 773
- Holman, C. C.**—Discussion on operative treatment of uncomplicated inguinal hernia, 533
- Holmes, G.**—Discussion on indications for use of radio-active thermal waters in Great Britain, 833
on spa treatment of pelvic disorders, 1426
- Horan, V. G.**—Discussion on effect of aural conditions on fitness for active service, 1533
- Hormone, thyrotropic, of hypophysis, hyperthyroidism and (A. Lœsner), 1445**
- Hormones in obstetrics and gynaecology, present position of, discussion on, 263**
- Horne, Jobson.**—Discussion on the problem of early laryngeal tuberculosis, 234
- Horse, purpuric conditions in, 723**
- Hosford, J. P.**—Arthrogram to show extent of synovial cavity after synovectomy, 1264
- Hospital records, mechanical tabulation of (B. E. Spear and C. A. Gould), 633**
tabulation of, nature of statistics obtained, 641
scope of, 643
- Howell, B. W.**—Discussion on prevention and treatment of ununited fractures, 993
- Howell, C. M. Hinds.**—Arachnoiditis, 33
- Howells, G. H.**—Discussion on orbital cellulitis due to sinus infection and its treatment, 1403
- Howitt, F.**—Discussion on indications for use of radio-active thermal waters in Great Britain, 832
- Hudson, J. R.**—Cutaneous streptothricosis, 1457
- Huggett, A. St. G.**—Discussion of therapeutic methods of arresting hæmorrhage, 645
- Human and animal diseases, epidemiology of (Sir F. Hobday), 835**
- Humerus, fractures of, musculospiral lesions in, 865**
- Humphreys, H. F.**—Three cases of osteomyelitis, 1241
- Hunt, E.**—Recurrent ulceration of mouth, 979
Superficial cicatrizing rodent ulcers of left upper eyelid, 1333
- Hunt, J. H.**—Reynaud's phenomenon in workmen using vibrating instruments, 171
- Hunter, John T.**—Discussion: impressions of anæsthesia in U.S.A. and Canada, 940
- Hurdon, E.**—Three cases of tumour of uterus, secondary to cystic ovarian tumours, 54
- Hutton, E. L., and Nicol, W. D.**—After-results of malaria therapy, 628
- Hydrocephalus, internal, following cerebral thrombosis in an infant, 768**
with syringomyelia, case of, 575
- Hydronephrosis, pathology of, recent observations on (W. E. Underwood), 817**
- Hyperthyroidism and the thyrotropic hormone of the hypophysis, 1445**
- Hypopharynx and cervical glands, carcinoma of, effect of deep X-ray therapy in, case of, 918**
- Ileitis, terminal (W. A. Jackman), 691**
- Immunization, active, against diphtheria by the combined subcutaneous and intranasal method (C. Jensen), 1117**
natural, in relation to epidemics, 59
- Industrial influences on the development of State Medicine (L. P. Lockhart), 91**
direct effects, 92
indirect effects, 96
- Infection, resistance to, influence of nutrition in, 1039 et seq.**
role of Vitamin C in relation to, 1044, 1045
susceptibility to, factors influencing, 1046
- Infectious disease, effects of nutrition on, discussion on, 1039**
malnutrition and, 64
See also Epidemics.
- Influenza, blindness after, two cases of, 704**
- Influenzal meningitis with complete recovery, case of, 707**
- Infraclavicular plexus trunk involvement in dislocations of shoulder-joint, 864**
- Inguinal hernia, uncomplicated, operative treatment of, discussion on, 529**
- Inhalators in treatment of asphyxia neonatorum, 1467**
- Innervation of the periodontal membrane, comparative study of (W. Lewinsky and D. Stewart), 1355**
- Innes, J. R. M.**—The lesions produced in the organs of the rabbit by single and repeated injections of B.C.G.: a preliminary note, 887
- Insectivora, innervation of periodontal membrane in, 1363**
- Insteps and soles, atrophic areas on, with ? telangiectasis: case for diagnosis, 984**
- Intestine, large, investigation of, methods of, 1384**
small, investigation of, special methods of, 1380
- Intestines, malrotation of, in child aged 9 months: cured by operation, 405**
- Intracranial aneurysm, traumatic, case of, 854**
- Intratracheal insufflation in treatment of asphyxia neonatorum, 1469**
- Intravenous resuscitation in treatment of asphyxia neonatorum, 1469**
- Iris, free border of, tubercle on, 950**
melanoma of (? malignant), case of, 701
- Ironside, R.**—Acute syphilitic meningitis with papilloedema, 576
Hydrocephalus with syringomyelia, 575
- Irradiation, pre- and post-operative, value of, in malignant disease, discussion on, 1173**

- Jackman**, W. A.—Terminal ileitis, 691
- Jacobs**, A.—Discussion on the Harris operation and its modifications, 1231
- Jacobsohn**, F.—? Lupus erythematosus, 368
Parapsoriasis treated with thorium X, 366
Tubercloid leprosy, 1054
and **Heggs**, G. B. M.—Poikiloderma with parapsoriatic spots treated with thorium X, 367
- Jakob's** syndrome (senile dementia with Parkinsonism), 1100
- James**, W.—Cases of: (1) Multilocular cyst; (2) Squamous-celled carcinoma; (3) Extensive osteomyelitis of mandible; (4) Papillomata of palate; (5) Fibrous epulis between 2 & 1; (6) Dilated composite odontome; (7) Dental cyst (right mandible); (8) Large dental cyst arising in left maxilla and obstructing the nose, 1246
- Jaundice**, familial, acholuric, in the third (? fourth) generation of manifestation of the disease, 1073
- Jeffcoate**, T. N. A.—Discussion on the present position of hormones in obstetrics and gynaecology, 270
- Jefferson**, G.—Colloid cyst of third ventricle, 850
Two cases of left frontal lobectomy, 851
- Jenson**, C.—Active immunization against diphtheria by the combined subcutaneous and intranasal method, 1117
- Jewesbury**, R. C.—Cleido-cranial dysostosis, 882
- Jobson**, T. B.—Unilateral choanal atresia in a woman, aged 23, 917
- "**Johnin**," in diagnosis of paratuberculosis of cattle and sheep, 85, 86
- Johne's** disease. See Paratuberculosis.
- Johnson**, K. S., **Wilson**, R. A., and **Torrey**, M. A.—The initiation of respiration in asphyxia neonatorum, 1461
- Joly**, J. Swift.—Four specimens of tumour of renal pelvis, 465
- Jones**, A. Rocyn.—Degeneration of carpus produced by use of a compressed air-drill, 210
- Jones**, D. B. S. Bruce, and **Wigley**, J. E. M.—Case clinically resembling morphea, with a tuberculous background and indeterminate histology, suggestive of necrobiosis lipidica, 737
- Jones**, Grace M.—Investigation into the ocular changes in normal and hypertensive pregnancy, 1286
- Jones**, W. H. S.—The Scientist's Playground, 859
- Jory**, P.—Discussion on effect of aural conditions on fitness for active service, 1536
- Juler**, F. A.—Melanoma (? malignant) of iris, 701
- Juxtapapillary** choroiditis (Jensen) case of, 948
- Kayser-Fleischer** ring, Wilson's disease with, case of, 858
- Kennedy**, E. M.—? Cerebro-macular degeneration, 388
- Keratoderma** climactericum (Haxthausen) treated with oestrone, 738
- Keratitis** punctata, case of, 198
- Kerion**, resolving, ? case of, 521
- Kerr**, J. M. Munro.—Discussion on relative value of upper- and lower-segment Cæsarean operations, 560
- Kerridge**, P. M. T.—Discussion on labyrinthine reactions and their relation to the clinical tests, 914
Hearing and speech in deaf children, 1494
chronic rheumatism, 611
- ***Kersley**, G. D.—The peripheral circulation in chronic rheumatism, 611
- Keynes**, G.—Discussion on operative treatment of uncomplicated inguinal hernia, 529
- Keyes**, M.—Discussion on spa treatment of pelvic disorders, 1419
- Kidney**, adeno-carcinoma of, five cases of, 463
adenoma of, large, with hemorrhage into growth, 453
- ***Kidney**, Grawitz tumours of, origin of, and the frequency of gastric ulcer-cancer: the search for truth with special reference to (W. D. Newcomb), 113
non-malignant tumours of, necessitating nephrectomy (C. Dukes), 447
one, multiple diseases in, 467
pelvis of, multiple papillomata filling, 453
tuberculosis, diagnosis of, renal occlusion in relation to, 1434, 1435
healing of lesions of, 1433
- Kidneys**, both, ureters and bladder, papillomata of, due to bilharzial infection, 451
See also Renal.
- Kindersley**, C. E.—Cirroid aneurysm involving tongue and floor of mouth, 709
Fractured os calcis, 1257
Fractures of tibial tuberosities, 1255
Reconstruction of thumb, 1260
- King**, E. F.—Epithelial growths of conjunctiva and cornea, 1273
- Klaber**, R.—? Chloasma virginum periorale, 1057
Lichen nitidus, 1056
sclerosus et atrophicus (Hallopeau), 977
Molluscum contagiosum miliare (Whitfield), 31
Necrobiosis lipidica diabetorum, 976
Sebocystomatosis (Günther), 976
- Knee-joint**, function of, effect on of removal of patella for simple transverse fractures (R. Brooke), 203
internal derangement of, in children and adolescents (H. A. T. Fairbank), 427
ligamentous ruptures of, external popliteal lesions in, 867
- Konstam**, G.—Purpura and aplastic anemia, 727
- Krestin**, M.—Sclerema neonatorum: localized type, 412
- Labio-buccal** melanosis, case of, 520
- Labour**, self-induction of analgesia during, new type of nitrous-oxide machine for (J. Chassar Moir), 1281
- Labyrinth**, concussion of, modern views of (N. Rh. Blegvad), 321
function of, some observations on (I. A. Tumarkin), 599
tests, sources of error in rotation test, 599
- ***Labyrinthine** reactions and their relation to the clinical tests (W. J. McNally), 905
characteristic reaction patterns of body musculature, 908

- Labyrinthine** reactions and their relation to the clinical tests, elimination of individual labyrinthine end-organs, 908
intracranial connexions from the labyrinth, 911
mechanism of semicircular canal stimulation, 908
mechanism of utricular stimulation, 909
reactions following the vestibular tests, 912
the rapid tilt test, 907
the sacculi, 911
the two modes of utricular stimulation, 909
- Labyrinthitis**, chronic; fracture of mastoid process, involving facial canal, 424
- Lapage, C. P., and Wilson, D. S. P.**—Tumour of spinal cord in child aged 2½ years: specimen, 1185
- Laryngeal** intubation and insufflation in treatment of asphyxia neonatorum, 1468
tuberculosis, conditions significant of, 223-230
conditions simulating, 222, 223
diagnosis of, 222
early, the problem of, discussion on, 221
- Larynx**, carcinoma of, laryngectomy for, with development of secondary gland nearly five years after original operation, 1393
human, structure of, evidence of comparative anatomy on (V. E. Negus), 1394
- Laurence-Moon-Biedl** syndrome, three cases of, 388
- Lavine, L., and Upcott, H.**—Myocardial ischaemia treated by graft of skeletal muscle to the heart, 772
- Law, Frank W.**—Two cases of "post-influenzal" blindness, 704
- Layton, T. B.**—Discussion on choice and technique of anaesthetics for nose and throat operations, 923
- Le Mée, J. M.**—Oto-mastoiditis in infants, 1293
- Lens**, tremulous, transitory, 945
- Leprosy**, tuberculoid, case of, 1054
- Leptospira**, serological differentiation of, in Weil's disease, 752
- Lett, H.**—Discussion on genito-urinary tuberculosis, 1443
- Leukæmic** erythrodermia, case of, 192
- Leucosis**, reticulo-endothelial, of fowls ("erythro-leucosis") (H. P. Bayon), 377
- Leucoplakia** vulvæ, partial resolution of, under oestrin therapy, 1330
- Levitt, W. M.**—Discussion on value of pre- and post-operative irradiation in malignant disease, 1175
- Lewinsky, W., and Stewart, D.**—Comparative study of the innervation of the periodontal membrane, 1355
- Leyton, O.**—Discussion on protamine insulinate, 813
- Lichen** nitidus, case of, 1056
planus associated with atrophy of nail matrix and hair follicles of scalp, 198
atrophicus, ? case of, 735
with vesicular onset, case of, 736
? case of, for diagnosis, 1060
involving the mouth, 499
sclerosus et atrophicus (Hallopeau), 977
- Lightwood, R.**—Sclerema neonatorum: localized type, 412
- Limbs**, lower, inequality of length in, bone shortening for (R. Brooke), 441
- Lipæmia**, splenomegaly with, case of, 711
- Lipodystrophia** progressiva, case of, 1071
- Livingston, P. C.**—Retinitis pigmentosa in a young airman, 705
Tuberculosis or metastatic choroiditis, 706
- Lloyd, E.**—Discussion on prevention and treatment of ununited fractures, 993
- Lobectomy**, frontal, left, two cases of, 851
occipital, case of, 853
- Lobeine**, injection of, into umbilical vein for resuscitation in asphyxia neonatorum, 1470 *et seq.*
- Lockhart, L. P.**—Industrial influences on the development of State Medicine, 91
- Lockhart-Mummery, J. P.**—Discussion on medical treatment of chronic ulcerative colitis, 360
- Loeser, A.**—Hyperthyroidism and the thyrotropic hormone of the hypophysis, 1445
- Luker, S. Gordon.**—Circumscribed polypoid sarcoma of cervix uteri, 49
Tubal pregnancy associated with (or caused by) an ovarian cyst, 50
- Lumsden, R. B.**—Discussion on otitis media in early childhood, 1314
- Lung**, actinomycosis of, 876
decortication of, for tuberculous pleurisy, 168
lower lobe collapse, with bronchial dilatation: apparent resolution, case of, 107
- Lungmotors**, pulmotors and resuscitators in treatment of asphyxia neonatorum, 1466
- Lupus** erythematosus, ? case of, 368
vulgaris of nose under treatment with tuberculin, 26
with cutaneous horns, case of, 1337
- Lyle, T. Keith.**—Hemispherical formations in Bowman's membrane, 701
- Lymphadenoma**, ætiology and diagnosis of, discussion on, 541
biological test for, 541
use of sensitized vaccine in, illustrative cases, 544-549
principle and mode of preparation, 542
- Lymphogranuloma**, benign, case of, 1329
- Lymphogranulomatosis**, benign, with ocular symptoms, case of, 1057
- McAlpine, D.**—Serous meningitis, secondary to tonsillitis, 395
Tumour of left cerebellar lobe, 395
- McArdle, M. J.**—Wilson's disease with Kayser-Fleischer ring, 568
- Macbeth, A. N.**—Partial resolution of leukoplakia vulvæ under oestrin therapy, 1331
- MacCormac, H.**—Discussion on specific treatment of staphylococcal infections, 518
Molluscum sebaceum, 1053
and Whitby, L. E. H.—Leukæmic erythrodermia, 192
- MacDonald, A. D.**—Discussion on neurological sequelæ of spinal anaesthesia: experimental and pharmacological considerations, 1015
- MacGregor, T. N.**—Discussion on the present position of hormones in obstetrics and gynaecology, 272

- McIlroy, Louise.**—Discussion in relative value of upper- and lower-segment Caesarean operations, 562
Results of radium treatment in (1) carcinoma of uterus; (2) uterine hæmorrhage, 1345
- McInnes, R. G.**—Observations on heredity in neurosis, 895
- Macintosh, R. R.**—Discussion: impressions of anaesthesia in U.S.A. and Canada, 937
- Mackay, H. M. M. and O'Flynn, E.**—Tuberosc sclerosis with rhabdomyomata in the heart: pathological specimens, 1063
- McNally, W. J.**—Effect of deep X-ray therapy in case of carcinoma of hypopharynx and cervical glands, 918
- *McNally, W. J.**—Labyrinthine reactions and their relation to the clinical tests, 905
- Macular degeneration** in patient aged 24, 390
- Madelung's deformity**, and similar conditions, an operation for the correction of (H. J. Burrows), 565
- Magill, I. W.**—Discussion: impressions of anaesthesia in U.S.A. and Canada, 943
on choice and technique of anaesthetics for nose and throat operations, 930
- Maitland-Jones, A.**—Epi-tuberculosis showing also bone lesions, 711
- Malarial therapy**, after-results of, 628
in general paralysis: a follow-up study of (J. E. Nicole and G. J. Harrison), 623
clinical results, 623
late results of, 623
results from the Maudsley Hospital (T. Tennant), 631
- Malignancies**, advanced, management of, 773
- Malignant disease**, biopsy in, 305
causation in, 301
diagnosis in, 305
management of, the debatable land in (G. Grey Turner), 301
pre-cancerous conditions in, 302
preparation for operation in, 318
propaganda in, 301
questions of treatment in, 307
results of operative treatment in, 309
so-called inoperable cases of, 318
technique of operations for, 315
value of pre- and post-operative irradiation in, discussion on, 1173
metastases, distant, treatment of, 779
tumours of bone, discussion on, 781
- Malnutrition and infectious disease**, 64
- Man and animals**, purpuric conditions in, discussion on, 715
- Mandelate (sodium and ammonium)** as urinary antiseptic, discussion on, 501
- Mandible**, alveolar ridge of, squamous-celled carcinoma of, 1247
multilocular cyst of, 1246
osteomyelitis of, extensive, 1248
subacute, 1241
two cases of, 1244
- Mange**, epidemiology of, 839
- Manson-Bahr, P. H.**—Comparative medicine and its relation to the study of tropical medicine, 237
Discussion on medical treatment of chronic ulcerative colitis, 360
- Manson-Bahr, P. H.**—Notes on some landmarks in tropical medicine, 1181
- Marnham, R.**—Discussion on medical treatment of chronic ulcerative colitis, 361
- Marshall, C. M.**—Discussion on relative value of upper- and lower-segment Caesarean operation, 561
- *Marshall, G. Struan.**—Respiration in high-flying, 995
- Martin, G. E.**—Discussion on effect of aural conditions on fitness for active service, 1537
- Martin, J. Purdon.**—Discussion on mental disorder following head injuries, 1094
on neurological sequelæ of spinal anaesthesia, 1032
Traumatic intracranial aneurysm, 854
- Martindale, L.**—Discussion on results of radium treatment in carcinoma of cervix, 1352
- Mason, G. A.**—Angina pectoris treated by cardio-mentoexy, 762
Four typical cases after pneumonectomy for bronchiectasis, 760
- Mastoid asymmetry**, three cases of, 423
operations, radical, deafness after, characteristics of, 1486
- Matthew, A. W.**—Discussion on choice and technique of anaesthetics for nose and throat operations, 926
- Maudsley Hospital**, results of malarial therapy from, 631
- Maurer, G.**—Discussion on treatment of pleural effusions, 843
- Maxilla**, fibrous hypertrophy of, 1252
superior, chronic osteomyelitis of, 1242
- Mayo operation**, modified, for proclitencia (E. Williams), 1282
- Mechanical tabulation of hospital records**, nature of statistics obtained, 641
scope of, 643
- Meckel's diverticulum** causing severe recurrent hæmorrhage from the bowel, case of, 1220
- Mediastinal ganglio-neuroblastoma**, case of, 1195
tumours, differential diagnosis of (N. L. Rusby), 1205
- Medicine and Science (T. A. Ross)**, 179
and science in the writings of Smollett (E. A. Underwood), 961
comparative, and its relation to the study of tropical medicine (P. H. Manson-Bahr), 237
the aims of, 189
- Medico-biological investigation**, value of morphology in, an example of (E. L. Taylor), 238
- Medulloblastoma of fourth ventricle** with repeated spinal recurrences, 396
- Megaduodenum**, specimen of, 875
- Megalencephaly**, case of, 391
- Melanoma** (? malignant) of iris, case of, 701
- Melanomata**, metastasizing, multiple, 1393
- Melanosis**, labio-buccal, case of, 520
- Ménière's syndrome**, types of attack in, 606
- Meningitis**, associated, in otitis media, 1307
influenzal, with complete recovery, 707, 877
serous, secondary to tonsillitis, 395
streptococcal, followed by recovery, 411
syphilitic, acute, with papilledema, case of, 576

- Mennell, Z.**—Discussion on choice and technique of anaesthetics for nose and throat operations, 930
- Mental** disorders following head injury, (C. P. Symonds), 1081
- Metabolic** disorders, treatment of, by radio-active thermal waters in Great Britain, 830
- Metastases**, malignant, distant, treatment of, 779
- Metrochylorrhœa**, case of, 50
- Meyerhof, Max.**—An early mention of sleeping sickness in Arabic literature, 670
- Micturition**, functions of, variations in, following injury to spinal cord, 1233
- Miliary** tuberculosis, chronic (J. M. Vaisey), 1208
- Milk** as a factor in the cause of disease, discussion on, 951
(cows), infection of, human diseases spread through, 955
- Mill, W. A.**—Basal-celled carcinoma of palate, 922
- Milligan, E. T. C.**—Discussion on operative treatment of uncomplicated inguinal hernia, 537
- Minett, F. C.**—Discussion on milk as a factor in the cause of disease, 957
- Minton, J.**—Cases of: (1) Retinitis pigmentosa sine pigmento. (2) Retinitis pigmentosa cum punctata albescens. (3) Retinitis pigmentosa. (4) An old case of neuro-retinitis (probably syphilitic) and closely simulating retinitis pigmentosa, 385, 386
Clinical study of fifty-four cases of occlusion of central artery of retina and its branches, 285
- Mitchiner, P.**—Discussion on operative treatment of uncomplicated inguinal hernia, 536
- Mitral** stenosis with congestive heart failure treated by complete thyroidectomy, 157
- Moir, J. Chassar.**—A new type of nitrous-oxide machine for self-induction of analgesia during labour, 1281
Discussion on relative value of upper- and lower-segment Cæsarean operations, 561
- Molluscum** contagiosum miliare (Whitfield), case of, 31
sebaceum, case of, 1053
- Moore, A. M. A.**—Discussion on prevention and treatment of ununited fractures, 987
- Morgan, B.**—Relation of the ear, nose and throat to the diseases of children, 1415
- Morphœa** with a tuberculous background and indeterminate histology, suggestive of necrobiosis lipoidica, case clinically resembling, 737
- Morphology**, value of, in medico-biological investigation, an example of (E. L. Taylor), 238
- Morris, I. B., Sorsby, A., Elkeles, A., and Goodhart, G. W.**—Experimental staining of retina in life, 1271
- Morson, A. C.**—Discussion on urinary antiseptics, 513
Large ureteric calculus, 1078
Papillomata of both kidneys, ureter and bladder due to bilharzial infection, 451
The Harris Operation and its modifications, 1223
- Mougeot, A.**—Discussion on spa treatment of pelvic disorders, 1426
- Mouse**, innervation of periodontal membrane in, 1361
- Mouth**, lichen planus involving, 499
ulceration of, recurrent, 979
- Moyle, R. D.**—Papulo-necrotic tuberculide, 528
- Muir, D. C.**—Discussion on course and management of congenital heart disease, 698
- Muir, E. G.**—Resection of œsophagus and cardia, 162
- Musculospiral** lesions in fractures of humerus, 865
- Mustard** gas burns, delayed corneal ulceration following, 949
- Mycosis** fungoides, cases of, 191, 364, 367
- Myeloma**, plasma-celled, solitary, of vertebral body, causing paraplegia, 931
- Myelomalacia** following spinal anaesthesia, 1024
- Myers, B.**—Discussion on purpuric conditions in man and animals, 728
- Mygind, S. H.**—Discussion on orbital cellulitis due to sinus infection, and its treatment, 1400
on physical aspects of tinnitus, 1518
on relation of ear, nose and throat to the diseases of children, 1417
and **Dederding, D.**—Some problems of aural medicine, 1485
- Myocardial** ischaemia treated by graft of skeletal muscle to the heart, 772
- Myositis** ossificans progressiva, case of, 162
- Nævus**, follicular, symmetrical, 370
- Nail** dystrophy, case of, 1341
- Nailbed**, capillaries in, condition of, in normal and rheumatic conditions, 616-619
- Naish, A. E.**—Discussion on therapeutic methods of arresting hæmorrhage, 650
- Necrobiosis** lipoidica diabeticoorum, cases of, 527, 976
- Negus, V. E.**—The evidence of comparative anatomy on the structure of the human larynx, 1394
- Neilson, D. F. A.**—Discussion on choice and technique of anaesthetics for nose and throat operations, 928
- Nephrectomy**, non-malignant tumours of kidney necessitating (C. Dukes), 447
- Nerve-anastomosis** in animals, results of experiments in, 874
- Nerve** injuries due to penetrating wounds, 868
- Nerves**, peripheral, injuries of, discussion on, 863
results of electrical stimuli to, 871
- Neuritis**, fifth-nerve, following trauma, case of, 392
- Neurological** approach to psychiatry, 186
disease, precipitated by spinal anaesthesia, symptoms of, 1011
sequelæ of spinal anaesthesia, 1007
- Neuro-retinitis**, old case of (probably syphilitic), and closely simulating retinitis pigmentosa, 386
- Neurosis**, heredity in, observations on (R. G. McInnes), 895
- Neutropenia**, rhythmical, with recurrent buccal ulceration, 980
- Neville, W. S. T.**—Discussion on choice and technique of anaesthetics for nose and throat operations, 924

- Neville, W. S. T.**—Discussion on orbital cellulitis due to sinus infection and its treatment, 1406
on physical aspects of tinnitus, 1518
on some problems of aural medicine, 1493
- Nevin, S.**—Fifth-nerve neuritis following trauma, 392
Secondary syringomyelia. ? Vertebral aneurysm, 574
- Newborn** infants suffering from asphyxia pallida, resuscitation of, summary of important facts concerning, 1478-1481
retinal hæmorrhages in (F. Richman), 277
- *Newcomb, W. D.**—The search for truth, with special reference to the frequency of gastric ulcer-cancer and the origin of Grawitz tumours of the kidney, 113
- Newns, G. H.**—Collapse of lower lobe with bronchial dilatation: apparent resolution, 107
Complete transposition of viscera, 884
Hepatomegaly ? cause, 1069
- Nicholls, M. F.**—Discussion on operative treatment of uncomplicated inguinal hernia, 557
- Nicol, W. D., and Hutton, E. L.**—After results of malaria therapy, 628
- Nicole, J. E., and Harrison, G. J.**—A follow-up study of general paralysis with special reference to malarial therapy, 623
- Nitrous-oxide** machine, new type of, for self-induction of analgesia during labour (J. Chassar Moir), 1281
- Noble, R. L.**—The action of pituitary extracts on gastric secretion, 815
- Nodules.** ? tuberculous, case of, 733
- Nonne-Milroy-Meige** œdema, of late onset, in sisters, case of, 933
- Nose** and throat operations, anæsthetics for, choice and technique of, discussion on, 923
lupus vulgaris of, under treatment with tuberculin, 26
throat and ear, relation of, to the diseases of children (B. Morgan), 1415
- Nutrition** and its effects on infectious disease, discussion on, 1039
- Obstetrical,** gynecological and genito-urinary practice, Arabian, illustrated from Albu-casis (M. S. Spink), 653
- Obstetrics** and gynecology, present position of hormones in, discussion on, 263
- Occipital** lobectomy, case of, 853
- Ocular** changes in normal and hypertensive pregnancy, investigation into (G. M. Jones), 1286
torticollis, two cases of, 1264
- O'Donovan, W. J.**—Black hairy tongue: specimen, 732
Discussion on specific treatment of staphylococcal infections, 520
- O'Donoghue, J. G.**—Unusual deformity of genitalia, 1193
- Odontome,** composite, dilated, 1250
- Œsophagoscopy,** simplified: œsophagoscopy without anæsthesia, without head-rest and without assistance (S. Belinoff), 496
- Œsophagus,** investigations of, special methods of, 1378
lower, and cardia, resection of, case of, 162
- Estrin** therapy causing partial resolution of leukoplakia vulvæ, 1330
- O'Flynn, E., and Mackay, H. M. M.**—Tuberose sclerosis with rhabdomyomata in the heart; pathological specimens, 1063
- Ogilvie, W. H.**—Discussion on malignant tumours of bone, 800
on operative treatment of uncomplicated inguinal hernia, 532
- Operating** theatre, ideal structure of, from the point of view of an anæsthetist (G. Edwards), 331
- Ophthalmoplegia** externa, bilateral, congenital: a case helped by prisms, 43
- Ophthalmoplegie** migraine, case of, 387
- Optic** atrophy, primary, bilateral, from glioma of optic nerves, 855
nerve, chiasma and thalamus, tumour of, 1096
- Orbit,** vascular growth of, hæmorrhage from, ? case of, 946
- Orbital** cellulitis due to sinus infection, and its treatment, discussion on, 1397
- Orbits,** both, revolver-shot through, 390
- Ormerod, F. C.**—Discussion on effect of aural conditions on fitness for active service, 1537
on labyrinthine reactions and their relation to the clinical tests, 914
on relation of ear, nose and throat to the diseases of children, 1417
on the problem of early laryngeal tuberculosis, 233
- Os calcis,** fractured, case of, 1257
- Osteo-arthritis** of right hip, treated with an extra-articular bone graft. Osteo-arthritis of the right knee, treated with auto-fat injection, 757
- Osteogenic** sarcoma, discussion on, 800
- Osteomyelitis** of mandible, two cases of, 1244
three cases of, 1241
vitamin C in relation to, 1045
- Otitis** media in children, age of onset of, 1495
in early childhood, discussion on, 1293
incidence of, 1297
prophylaxis, 1307
relation of, to sinusitis, 1301
suppurative, deafness of, characteristics of, 1487
various organisms found in, incidence of, 1302
- Oto-mastoiditis** in infants, 1293
- Otosclerosis,** deafness in, characteristics, 1486
surgical treatment of, comparison between two procedures, 1521
indications for, 1521
mechanisms of two procedures, 1520
procedures based on acoustic results of labyrinthine fenestration, 1519
depending on pathogenesis, 1519
the present position of (M. Sourdille), 1519
- Ovarian** cyst, tubal pregnancy associated with (or caused by), 50
- Ox,** purpura hæmorrhagica in, 726
- Oxycephaly** showing Apert's syndrome, case of, 387
showing Crouzon's syndrome, two cases of, 387

- Paget's disease** affecting left femur only, case of, 157
of skull associated with a pituitary neoplasm, 849
- Palate**, basal-celled carcinoma of, case of, 922
papilloma of, 1249
- Palmer, A. C.**—The prolapse syndrome, 1353
- Pancreas**, investigation of, special methods of, 1379
- Panton, P. N.**—Specific treatment of staphylococcal infections, 515
- Papillomatosis**, diffuse: removal of kidney, ureter, and part of bladder, 448
- Parapsoriasis** treated with thorium X, 366
- Parasitic aberrancy** and new diseases, 67
mutation: a cause of epidemics, 66
variation in epidemics, 64
- Paratuberculosis** in cattle and Sheep (G. W. Dunkin), 83
causal organism of, 84
diagnosis of, 85
incubation period of, 87
geographical distribution, 83
post-mortem examination, 84
prevention of, 87
- Parish, H. J.**—Discussion on specific treatment of staphylococcal infections, 519
- Parker, G.**—Multiple diseases in one kidney, 467
- Parodontal infection**, elimination of, 1164
pockets, sterile filtrate from, toxicity of (J. W. Graham), 1165
- *Parodontal sulcus**, infection of, local and remote sequelæ of (E. W. Fish), 1149
- Patella**, removal of, for simple transverse fractures, effect on function of knee-joint (R. Brooke), 203
- Paterson, D.**—Actinomycosis of lung, 876
Undulant fever, case of, 880
Werdnig-Hoffmann paralysis in the elder of twins, 1071
- Paterson, R. S.**—Methods of investigating the large intestine, 1384
- Patterson, N.**—Carcinoma of tongue, followed by cystic adenoma of thyroid, 1393
Laryngectomy for carcinoma of larynx, with development of secondary gland nearly five years after original operation, 1393
Multiple metastasizing melanomata, 1393
- Payne, W. W.**—Discussion on urinary antiseptics, 510
- Pearson, S. Vere.**—Discussion on treatment of pleural effusions, 848
- Pelvic disorders**, spa treatment of, discussion on, 1419
- Pemphigus**, erythema multiforme type of, 369
- Perception** deafness, characteristics of, 1485
- Pericarditis**, constrictive, chronic (Pick's syndrome), report and specimen, 764
- Periodontal membrane**, innervation of, comparative study of (W. Lewinsky and D. Stewart), 1355
- Periapillary choroidal sclerosis**, two cases of: a familial group, 386
- Peripheral embolectomy** (V. H. Riddell), 684
nerves, injuries of, discussion on, 863
- Perry, C. Bruce.**—Discussion on course and management of congenital heart disease, 693
- Peters, A. D. K.**—Case of angioma serpiginosum, 363
Granulosis rubra nasi, 1054
Partial resolution of leukoplakia vulvæ under œstrin therapy, 1330
- Pharynx**, investigation of, special methods of, 1378
- Phenolphthalein** eruption, case of, 1059
- Phlebectasia**, case of, 521
- Phosgene**, effects of, on respiratory system, 1033, 1035
- Pick's syndrome** (chronic constrictive pericarditis), report and specimen, 764
two cases of, 763, 1073
- Pilosebaceous** follicles and sebaceous secretion, changes in, following herpes zoster, 975
- Pituitary** extracts, action of, on gastric secretion (E. C. Dodds and R. L. Noble), 815
- Pityriasis** lichenoides et varioliformis acuta, case of, 191
rubra pilaris, case of, 200
- Platt, H.**—Discussion on injuries of peripheral nerves, 863
- Pleural effusion**, treatment of, discussions on, 843
- Pleurisy**, tuberculosis, decortication of lung for, 168
- Plummer, N. S.**—Purpura associated with bronchiectasis, 23
- Pneumatic instruments.** See vibrating instruments
- Pneumectomy**, for bronchiectasis, four typical cases of, 760
- Pneumonia** in children, incidence of otitis media in, 1305
staphylococcal, case of, specimen from, 885
- Poikilo-dermato-mycosis**, case of, 194
- Poikiloderma** with acrosclerosis and muscular wasting, 1334
with parapsoriatic spots treated with thorium X, 367
- Polioencephalitis hæmorrhagica superior**, case of, 1096
- Polyposis** of stomach, 1373
- Polyserositis**, case of, 766
- Population**, density and rate of, change of, in relation to epidemics, 62
- Porritt, A. E.**—Endothelioma of tibia (with pathological fracture), 766
- Potter, B.**—Discussion on effect of aural conditions on fitness for active service, 1536
- Potter, C. T.**—Hepato-splenomegaly: ? idiopathic cirrhosis, 409
- Poulton, E. P.**—Discussion on urinary antiseptics, 513
- Pregnancy**, intra- and extra- uterine, excision of extra-uterine pregnancy in fourth month, together with the rudimentary horn of the uterus, followed by full-term delivery of the intra-uterine pregnancy, 562
intra-uterine and extra-uterine, combined, 562
normal and hypertensive, investigation into ocular changes in (G. M. Jones), 1286
- Price, C. W.**—Air-conditioning in factories, 1544
- Price, R. E. A.**—Black hairy tongue: specimen, 732
- Pridie, K. H.**—Discussion on prevention and treatment of ununited fractures, 992

- Premunition** in relation to herd-immunity, 61
- Pringle, G. L. Kerr.**—Discussion on the peripheral circulation in chronic rheumatism, 620
- Pringle's disease** (adenoma sebaceum) with associated tumours of the nail-beds of the toes, 24
- Procidencia recti** present for twenty-three years and cured by operation, 1344
- uteri, carcinoma of cervix complicating, two cases of, 1343**
- complete, carcinoma of vagina complicating, 1483**
- modified Mayo operation for (E. Williams), 1282**
- Protamine insulinate (H. C. Hagedorn), 805**
- Prolapse syndrome, the (A. C. Palmer), 1353**
- Prostatectomy.** Harris operation for, and its modifications (C. Morson), 1223
- Pryce, D. M.**—Specimen of secondary carcinoma of ureters, 465
- Pseudo-xanthoma elasticum, case of, 199**
- Psychiatry,** neurological approach to, 186
- Psychological investigation, the matter of the private interview, 182**
- Psychology,** Freud and, 186
- quantitative results and, 185**
- Psychosis, traumatic, acute, 1081 *et seq.***
- Puberty, precocious, in a girl aged 4 years, 101**
- Purpura and aplastic anaemia, 727**
- associated with bronchiectasis, 23**
- haemorrhagia in the ox, 726**
- thrombocytopenic and non-thrombocytopenic, 715**
- Purpuras, classification and treatment of, 715**
- prognostic snake venom test of Peck and Rosenthal in, 718**
- treatment of, 719**
- Purpuric conditions in man and animals, discussion on, 715**
- Pyelography, retrograde, value of, in diagnosis of renal tuberculosis, 1437**
- Pyloric stenosis treated with eumydrine, two cases of, 1193**
- Rabagliati, D. S.**—Purpuric haemorrhagia in the ox, 726
- Rabbit, innervation of periodontal membrane in, 1361**
- Rabies, epidemiology of, 837**
- Radiation treatment of advanced malignancies, 773**
- Radiculitis, sacral, following spinal anaesthesia, 1010**
- Radiculomyelitis, following spinal anaesthesia, 1009**
- Radio-active thermal waters in Great Britain, indications for use of, discussion on, 827**
- Radiography in diagnosis of sinus thrombosis, a method of: sinography (P. Frenckner), 413**
- Radium treatment in (1) carcinoma of uterus; (2) uterine haemorrhage, results of, 1345**
- Ranken, D.**—Discussion on effect of aural conditions on fitness for active service, 1530
- Ray, M. B.**—Nodular rheumatism, 165
- Raynaud's phenomenon in workmen using vibrating instruments (J. H. Hunt), 171**
- Rectal cancer, histological grading of (C. Dukes), 371**
- after-history of each grade, 374**
- distribution of A B and C cases in each grade, 376**
- malignancy grades, 371**
- proportion of histological types, 372**
- Recto-sigmoid stricture, congenital, case of, 1192**
- Rectum, angioma of, case of, 1221**
- Renal pelvic epithelioma with massive calculi and no infection, 1075**
- growth, two specimens of, 448**
- pelvis, tumour of four specimens of, 465**
- tuberculosis, age-incidence of, 1430**
- classification of cases of, 1431**
- earliest symptom in, 1432**
- incidence of extra-renal tuberculosis, 1430**
- operative treatment of, 1438**
- tumours, three, successfully removed from female children aged 3 months, 4½ years and 14 years respectively, 449**
- See also under Kidney.*
- *Respiration in high flying (G. S. Marshall), 995**
- initiation of, in asphyxia neonatorum (R. A. Wilson, M. A. Torrey and K. S. Johnson), 1461**
- summary of important facts concerning, 1478-1481**
- system, effects of asphyxiating gases on, discussion on, 1033**
- tract, upper, infection of, relation of, to early bronchiectasis in children (J. H. Ebbs), 1407**
- Resuscitators in treatment of asphyxia neonatorum, 1466**
- Reticulo-endothelial leucosis ("erythroleucosis") of fowls (H. P. Bayon), 377**
- Retina, central artery of, and its branches, occlusion of, clinical study of fifty-four cases of (J. Minton), 285**
- experimental staining of, in life, 1271**
- Retinal changes in case of purpura, 946**
- haemorrhages in the newborn (F. Richman), 277**
- Retinitis exudativa externa? Sarcoma of choroid? 948**
- exudative, massive, ? case of, 46**
- pigmentosa, cases of, 385, 386**
- cum punctata albescens, case of, 385**
- in a young airman, case of, 705**
- sine pigmento, case of, 385**
- Retrobulbar neuritis. ? Devic's disease, case of, 394**
- Retroperitoneal hernias, 1374**
- Rhabdomyomata in the heart, tuberosc sclerosis with, pathological specimens, 1063**
- Rheumatic conditions, chronic, raw vegetable diet in, therapeutic trial of (D. C. Hare), 1**
- diseases, treatment of, by radio-active thermal waters in Great Britain, 829, 830**
- *Rheumatism, chronic, the peripheral circulation in (G. D. Kersley), 611**
- condition of capillaries in nailbed in, 617**
- nodular, case of, 165**
- Richardson, J. C.**—Spontaneous haematomyelia: report of two cases, one in association with an intramedullary angioma, and the other in association with syphilis, 1101

- Riches, E. W.**—Carcinoma of left ureter, 465
Discussion on the Harris operation and its modifications, 1232
on urinary antiseptics, 505
- Richman, F.**—Retinal hemorrhages in the newborn, 277
- Rickets, coeliac**, case of, 1074
- Riddell, V. H.**—Peripheral embolectomy, 684
- Ridley, F.**—Macular degeneration in a patient aged 24, 390
- Robb-Smith, T. A.**—Discussion on aetiology and diagnosis of lymphadenoma, 549
- Roberts, J. E. H.**—Chronic constrictive pericarditis (Pick's syndrome): report and specimen, 764
Polyserositis, 766
- Roche, A. E.**—Five cases of adeno-carcinomata of kidney, 463
- Rodent ulcer**, carcinoma derived from, massive involvement of skull in temporal and occipital regions by, case of, 916
superficial cicatrizing, of left upper eyelid, 1333
- Rodents**, innervation of periodontal membrane in, 1361
- Rodger, T. R.**—Discussion on otitis media in early childhood, 1294
- Rolleston, J. D.**—Discussion on epidemiology of animal and human diseases, 841
- Rosenheim, M. L.**—Discussion on urinary antiseptics, 501
- Ross, T. A.**—Discussion on mental disorder following head injuries, 1092
Medicine and Science, 179
- Rowlands, R. A.**—Pick's syndrome (pericardial), 1073
- Roxburgh, A. C.**—Discussion on specific treatment of staphylococcal infections, 519
? Lupus erythematosus, 368
- Rusby, N. Lloyd.**—The differential diagnosis of mediastinal tumours, 1205
- Russ, Sidney.**—Discussion on indications for use of radio-active thermal waters in Great Britain, 831
- Russell, D.**—Discussion on neurological sequelae of spinal anaesthesia, 1025
- Russell, Kerr.**—Discussion on short-wave therapy, 219
- Rushton, Martin A.**—Unilateral secondary facial cleft with excess tooth and bone formation, 79
- Sarcoma**, osteogenic, discussion on, 800
- Savage, W. G.**—Discussion on milk as a factor in the cause of disease, 951
- Savin, L. H.**—Cases of (1) Stargardt's disease; (2) Two cases of familial distichiasis; (3) Birth rupture of Descemet's membrane of left cornea; (4) Revolver-shot through both orbits, 390
- Scarff, R. W.**—Discussion on malignant tumours of bone, 796
- Schlüter, A., and Weber F. Parkes.**—Further report on case illustrating the action of bran in treatment of Hirschsprung's disease, previously shown Dec. 13, 1935, 107
Sebocystomatosis (Günther) in two brothers, 29
- Sciatica**, intractable, due to prolapsed intervertebral disc: treated by laminectomy, 1262
- Science and medicine** (T. A. Ross), 179
examination of the rules of, 182
the nature and methods of, 180
- Scientist's playground**, the (W. H. S. Jones), 859
- Scleredema adultorum** (Buschke), case of, 983
- Sclerema neonatorum**; localized type, case of, 412
- Scleroderma**, case of, 982
(or ? scleropanniculomyoderma), case of, 731
- Sclerosis**, diffuse, case of, 931
- Scott, C. E.**—Discussion on otitis media in early childhood, 1314
- Scott, McNair.**—Discussion on otitis media in early childhood, 1317
- Scott, S.**—Discussion on effect of aural conditions on fitness for active service, 1538
on function of the labyrinth, 609
on labyrinthine reactions and their relation to the clinical tests, 913
- Scott, W. M.**—Discussion on milk as a factor in the cause of disease, 958
- Sebocystomatosis** (Günther), case of, 976
in two brothers, 29
- Seddon, H. J.**—Coeliac rickets, 1074
Necrosis of head of femur following fracture of neck in a child, 210
Slipped femoral epiphysis, 572
- Semon, H.**—Labio-buccal melanosis, 520
Poikilo-dermato-myositis, 194
Poikiloderma with acrosclerosis and muscular wasting, 1334
- Sewer workers**, Weil's disease and, 752
- Shaw, W. Fletcher.**—Discussion on results of radium treatment in carcinoma of cervix, 1351
- Shanks, S. Cochrane.**—Discussion on some of the less common lesions and special methods of investigation of the alimentary tract and the influence of adjacent organs, 1377
- Sheen, A. W.**—Discussion on operative treatment of uncomplicated inguinal hernia, 536
- Sheep and cattle**, paratuberculosis in (G. W. Dunkin), 83
- Sheldon, W.**—Biliary cirrhosis with cyanosis and finger-clubbing, 406
Dermatomyositis, 109
Hypochromic anaemia, congenital heart disease, and peculiar facies, 1189
Specimen of congenital genito-urinary abnormalities with suprarenal enlargement, 1190
and **Edwards, H.**—Cirrhosis and jaundice: cholecystgastrostomy, 878
Congenital recto-sigmoid stricture, 1192
- Sherry-Dottridge, F.**—Nail dystrophy, 1341
- Ships** (H.M.'s) and Naval establishments, air-conditioning in, 1541
- Short-wave** therapy, discussion on, 211
- Shoulder-joint**, dislocations and fracture-dislocations, nerve injuries accompanying, 864
- Signy, A. G.**—Discussion on urinary antiseptics, 510
- Silcock, F. A. E.**—? Acne conglobata, 1338
Mycosis fungoids, 364
- Simpson, J. F.**—Massive involvement of skull in temporal and occipital regions by carcinoma derived from a rodent ulcer, 916

- Simpson-Smith, A.**—Chronic sinus of face, 1068
- Sington, H.**—Discussion on choice and technique of anaesthetics for nose and throat operations, 930
- Sinography**: a method of radiography in the diagnosis of sinus thrombosis (P. Freneckner), 413
- Sinus infection**, orbital cellulitis due to, and its treatment, discussion on, 1397
- thrombosis, diagnosis of, a method of radiography in: sinography (P. Freneckner), 413
- Sinusitis**, chronic, with early bronchiectasis, case of, 708
- relation of otitis media to, 1301
- Skin**, gangrene of, post-operative, progressive (A. M. Stewart-Wallace), 681
- staphylococcal infections of, specific treatment of (P. N. Pantan), 515
- superficial ulcerating tuberculosis of, 369
- Skull**, massive involvement of, in temporal and occipital regions by carcinoma derived from a rodent ulcer, 916
- Paget's disease of, associated with a pituitary neoplasm, 849
- Sleeping sickness**, an early mention of, in Arabic literature (M. Meyerhof), 670
- Smith, R. E.**—Discussion on imperfect migration of the testicle, 1327
- Smollet**, writings of, medicine and science in (E. A. Underwood), 961
- Snake venom**, its source, method of collection and uses (Sir W. Dalrymple-Champneys), 1453
- therapeutic uses of, 1453, 1454
- treatment of purpura by, 721
- Somerses, E. J.**—Three cases of corneal dystrophy, 389
- Soothill, V. F.**—Discussion on air-conditioning, 1549
- Soraby, A.**—Two cases of peripapillary choroidal sclerosis: a familial group, 386
- and **Avery, H.**, Three Cases of the Laurence-Moon-Biedl syndrome, 388
- Elkeles, A., Goodhart, G. W., and Morris, I. B.**—Experimental staining of retina in life, 1271
- Soulas, A.**—Bronchoscopytherapy in bronchopulmonary suppuration: its mechanism and results, 492
- Sound-conducting** affections, disturbances of vascular function in, 1488
- Sourdille, M.**—Discussion on some problems of aural medicine, 1492
- Present position of the surgical treatment of otosclerosis, 1519
- Souter, J. C.**—Clinical note on fungus infection of the skin of the feet, 1107
- Spa treatment** of pelvic disorders, discussion on, 1419
- Spear, B. E. and Gould, C. A.**—Mechanical tabulation of hospital records, 633
- Speech** and hearing in deaf children (P. M. T. Kerridge), 1494
- proficiency in, in deaf children, 1507
- Spina bifida occulta** with nervous symptoms: relieved by operation, 574
- Spinal anaesthesia**, neurological sequelae of, discussion on, 1007
- cord, tumour of, in child aged 2½ years: specimen, 1185
- injuries in war, treatment of bladder in (Sir J. Thomson-Walker), 1233
- Spink, Martin S.**—Arabian gynaecological, obstetrical and genito-urinary practice illustrated from Albusasia, 653
- Spleen**, X-rays to, in treatment of purpura, 719
- Splenomegaly**, transmissible, of fowls, or reticulo-endothelial leucosis ("erythroleucosis") (H. P. Bayon), 377
- with lipaemia, case of, 711
- Spriggs, Sir Edmund.**—The incidence and treatment of diseases of the colon, 1211
- Stableforth, A. W.**—Cutaneous streptothricosis: a case in Great Britain, 1455
- Staphylococcal infections**, specific treatment of (P. N. Pantan), 515
- Stargardt's disease**, case of, 390
- State Medicine**, development of, industrial influences on (L. P. Lockhart), 91
- Statistical tabulation**, processes of, applied to hospital records, 633
- Stebbing, G. F.**—Discussion on value of pre- and post-operative irradiation in malignant disease, 1178
- Stern, R. O.**—Localized symmetrical cortical sclerosis in an infant, 1095
- Tumour of the optic nerve, chiasma and thalamus, 1096
- Stewart, D. and Lewinsky, W.**—Comparative study of the innervation of the periodontal membrane, 1355
- Stewart, R. M.**—Amentia, familial cerebellar diplegia, and retinitis pigmentosa, 849
- Stewart, W.**—Discussion on orbital cellulitis due to sinus infection and its treatment, 1406
- Stewart-Wallace, A. M.**—Progressive post-operative gangrene of skin, 681
- Stomach**, investigation of, special methods of, 1378
- polyposis of, 1373
- sarcoma of, 1371
- Streptothricosis**, cutaneous (J. R. Hudson), 1457
- a case in Great Britain, 1455
- Stuart, A. M.**—Three cases exhibiting the Ehlers-Danlos syndrome, 984
- Sykes, W. S.**—Discussion: impressions of anaesthesia in U.S.A. and Canada, 942
- Symonds, C. P.**—Mental disorders following head injury, 1081
- Synovial cavity**, after synovectomy, arthrogram to show extent of, 1264
- Syringomyelia**, hydrocephalus with, case of, 575
- secondary. ? Vertebral aneurysm. Case of, 574
- Tabes dorsalis** with bilateral trigeminal neuralgia, case of, 573
- Talipes** varus resulting from defective tibial growth, Brockman's operation for, 207
- Tallerman, K. H.**—Influenzal meningitis with complete recovery, 707
- Taylor, E. L.**—An example of the value of morphology in medico-biological investigation, 238

- Taylor, H. J.**—Discussion on short-wave therapy, 213
- Teeth**, unusual structural abnormalities of, specimens from five cases of, 71
- Tennant, T.**—Discussion on mental disorder, following head injuries, 1092
Malarial therapy: results from the Maudsley Hospital, 631
- Testicle**, imperfect migration of; the surgical problem (G. G. Turner), 1319
- Thermal waters**, radio-active, in Great Britain, indications for use of, discussion on, 827
- Thomas, C. Hamblen.**—Physical aspects of tinnitus, 1512
- Thomas, J. M.**—Streptococcal meningitis, followed by recovery, 411
- Thompson, A. R. F. and Herbert, W. E.**—Research in gold casting, 245
- Thomson, F. G.**—Discussion on indications for use of radio-active thermal waters in Great Britain, 830
- Thomson, Sir St. Clair.**—Discussion and problem of early laryngeal tuberculosis, 231
- Thomson-Walker, Sir John.**—Treatment of the bladder in spinal injuries in War, 1233
- Thorium X**, parapsoriasis treated with, 366
poikiloderma with parapsoriatic spots treated with, 367
three-stage enema, 1382, 1383
- Throat** and nose operations, anaesthetics for, choice and technique of, discussion on, 923
nose and ear, relation of, to the diseases of children (B. Morgan), 1415
- Thrombocytopenic purpura** and non-thrombocytopenic purpura, 715
- Thumb**, reconstruction of, 1260
- Thyrotropic hormone** of hypophysis, hyperthyroidism and (A. Loesner), 1445
- Tibia**, endothelioma of (with pathological fracture, 766
obscure lesion in, case of, 202
- Tibial tuberosities**, fractures of, 1255
- Tinnitus**, estimation of head noises, 1517
extrinsic, 1512
intrinsic, 1515
noises of muscular origin, 1513
physical aspects of (C. Hamblen Thomas), 1512
vascular sounds in, 1514
- Todd, A. H.**—(1) Case for diagnosis: (2) protrusion acetabuli, 572
- Todd, T. F.**—Discussion on results of radium treatment in carcinoma of cervix and in uterine haemorrhage, 1352
Procidentia recti present for twenty-three years and cured by operation, 1344
Two cases of carcinoma of cervix complicating procidentia uteri, 1343
- Tombleson, J. B. L.**—? Gargoylism (chondro-osteo-dystrophy), 1070
- Tongue** and floor of mouth, cirroid aneurysm involving, 709
black, hairy: specimen, 732
carcinoma of, followed by cystic adenoma of thyroid, 1393
- Torrey, M. A., Wilson, R. A., and Johnson, K. S.**—The initiation of respiration in asphyxia neonatorum, 1461
- Torticollis**, ocular, two cases of, 1264
spasmodic, tic-like, with occasional upturning of the eyes, 398
- Toxoid**, use of, in treatment of staphylococcal infections, 516
- Trichoclasia**, idiopathic, ? case of, 527
- Trigeminal neuralgia**, bilateral, tabes dorsalis with, case of, 573
- Tropical medicine**, some landmarks in, notes on (P. H. Manson Bahr), 1181
- Trotter, G. C.**—Discussion on epidemiology of animal and human diseases, 841
- Tubal pregnancy** associated with (or caused by) an ovarian cyst, 50
- Tuberculide**, papulo-necrotic, case of, 528
two cases of, 735
- Tuberculin**, two cases of tuberculosis treated with, 935
- Tuberculosis**, bovine, incidence of infection with, 838
epidemiology of, 838
* genito-urinary, observations on (J. Carver), 1429
laryngeal, early, the problem of, discussion on, 221
miliary, chronic (J. M. Vaizey), 1208
pulmonary, vitamin C in relation to, 1045
surgical, vitamin C in relation to, 1045
- Tuberosc sclerosis** with rhabdomyomata in the heart; pathological specimens, 1063
- Tumarkin, I. A.**—Some observations on the function of the labyrinth, 599
- Turner, G. Grey.**—Discussion on operative treatment of uncomplicated inguinal hernia, 538
Imperfect migration of testicle: the surgical problem, 1319
The debatable land in the management of malignant disease, 301
- Turner, P.**—Discussion on operative treatment of uncomplicated inguinal hernia, 535
- Tympano-labyrinthopexy**, 110
- Tyrrell, T. M.**—Tubercle on the free border of iris, 950
- Upcott, H. and Lavine, L.**—Myocardial ischaemia treated by graft of skeletal muscle to the heart, 772
- Umbilical vein**, injection of lobeine into, for resuscitation in asphyxia neonatorum, 1470 *et seq.*
- Underwood, E. A.**—Medicine and science in the writings of Smollett, 961
- Underwood, W. E.**—Recent observations on the pathology of hydronephrosis, 817
- Undulant fever**, case of, 880
- United States of America and Canada**, anaesthesia in, impressions of, 937
- Ureter and Ureters**, carcinoma of, secondary, specimen of, 465
carcinoma of, with hydronephrosis and secondary growths in bladder, 453
left, carcinoma of, 465
papilloma and intussusception of, 456
primary papillomata of, secondary hydronephrosis and transplant deposits in bladder, Removal of kidney and ureter. Recovery, 449

- Ureters**, transplantation of, into pelvic colon, with total cystectomy, for malignant growth of bladder, based on seven successful cases (B. Ward), 137
- Ureteric calculus**, large, 1079
- Ureterocele**, three cases of, specimens from, 1078
- Urinary antiseptics** (including sodium and ammonium mandelate) discussion on, 501
- infection following injury to spinal cord, 1234
- tract, diseases of, treatment of, by radio-active thermal waters in Great Britain, 831
- Uroselectan**, value of, in diagnosis of renal tuberculosis, 1435
- Urticaria pigmentosa**, case of, 1059
- Uterine haemorrhage**, results of radium treatment of, 1345
- Uterus**, carcinoma of, results of radium treatment in, 1345
- intramural abscess of, following criminal abortion, 563
- the "prolapse syndrome" (A. C. Palmer), 1353
- tumour of, three cases of, secondary to cystic ovarian tumours, 54
- Uveo-parotitis**, case of, 947
- Vagina**, carcinoma of, complicating complete procidentia, 1483
- Vaizey, J. M.**—Chronic miliary tuberculosis, 1208
- Pick's syndrome (pericardial), 1073
- Vitamin C**, rôle of, in relation to infection, 1044
- Vegetable** (raw) diet in chronic rheumatic conditions, therapeutic trial of (D. C. Hare), 1
- Ventilation** conditions and their investigation, discussion on, 1541
- Ventricle**, third, colloid cyst of, 850
- Vertebral body**, solitary plasma-celled myeloma of, causing paraplegia, 931
- Vibrating instruments**, workmen using, Raynaud's phenomenon in (J. H. Hunt), 171
- *Vinyl** ether for dental anaesthesia (V. Goldman), 891
- indications and administration of, 892
- properties and toxicity of, 892
- Viscera**, transposition of, complete, 884
- Visual field defects**, congruous, due to congenital absence of nerve-fibres, 946
- Volvulus neonatorum**, exomphalus associated with: result six and a half years after operation, 881
- Waggett, E. B.**—Discussion on effect of aural conditions on fitness for active service, 1534
- Walker, F. A.**—Unilateral secondary facial cleft with excess tooth and bone formation, 79
- Walker, R. M.**—Decortication of lung for tuberculous pleurisy, 168
- Wallace, H. J.**—Specimen from case of staphylococcal pneumonia, 855
- Walter, W. Grey.**—The electro-encephalogram in cases of cerebral tumour, 579
- and **Wyllie, W. G.**—The electro-encephalogram in the diagnosis of cerebral pathology, 578
- Ward, B. J.**—Discussion on urinary antiseptics, 514
- Total cystectomy with transplantation of ureters into pelvic colon for malignant growth of urinary bladder (based on seven successful cases), 137
- Ward, R. Ogier.**—Discussion on urinary antiseptics 514
- Warner, E. C.**—Discussion of aetiology and diagnosis of lymphadenoma, 543
- Water**, immersion in, relation of Weil's disease to, 752
- Waters, R. W.**—Carbon dioxide absorption from anaesthetic atmospheres, 11
- Watkins, K.**—Discussion on treatment of bladder in spinal injuries in War, 1240
- Watkyn-Thomas, F.**—Discussion on function of the labyrinth, 609
- Discussion on physical aspect of tinnitus, 1518
- Watson-Williams, E.**—Chronic labyrinthitis; fracture of mastoid process, involving facial canal, 424
- Discussion on orbital cellulitis due to sinus infection and its treatment, 1406
- on otitis media in early childhood, 1317
- Perforation of aorta by swallowed foreign body: two specimens, 439
- Three cases of mastoid-asymmetry, 423
- Weber, F. Parkes.**—Ehlers-Danlos syndrome, 30
- Felty's syndrome (Chaufard-Still syndrome) 932
- Further report on case illustrating the action of bran in treatment of Hirschsprung's disease, previously shown Dec. 13, 1935, 107
- Sebocystomatosis (Günther) in two brothers, 29
- The Nonne-Milroy-Meige oedema, of late onset, in sisters, 933
- Tic-like spasmodic torticollis, with occasional upturning of the eyes, 398
- and **Anderson, R. G.**—A subcutaneous glomus tumour (Masson) in the little finger. Clinical account, 196
- and **Freudenthal, W.**—Nodular non-diabetic cutaneous xanthomatosis with hypercholesterolaemia and atypical histological features, 522
- Weil's disease**, carriers of the infective agent, 745
- causative organism of, 743
- fatality rates, 749
- geographical distribution of, 743
- incidence as regards sex and age, 749
- incubation time, 749
- relation of occupation to, 750
- relationship of saprophytic to pathogenic strains, 754
- route of infection in, 747
- seasonal incidence, 749
- serological differentiation of *Leptospira* in, 752
- *the epidemiology of (J. M. Alston and H. C. Brown), 741
- viability of the organism outside the animal body, 746
- Wellings, A. W.**—Specimens from five cases of unusual structural abnormalities of teeth, 71
- Wells, C. A.**—Discussion on genito-urinary tuberculosis, 1443

- Wells, C. A.**—Discussion on the Harris operation and its modifications, 1231
- Werdnig-Hoffmann** paralysis in the elder of twins, 1071
- Whitby, L. E. H., and McCormac, H.**—Leukæmic erythrodermia, 192
- Whitby, Morton.**—Discussion on the Harris operation and its modifications, 1232
- White, C.**—Discussion on spa treatment of pelvic disorders, 1425
- White, Duncan.**—Discussion on ætiology and diagnosis of lymphadenoma, 550
- Whitteridge, S. M.**—Benign lymphogranuloma, 1329
- Whittle, C. H.**—? Lichen planus atrophicus, 735
Nodules, ? tuberculous, 733
- Wigley, J. E. M.**—Atrophic areas on insteps and soles with ? telangiectases: case for diagnosis, 984
Pityriasis rubra pilaris, 200
Purpura associated with bronchiectasis, 23
and **Jones, D. B. S. Bruce.**—Case clinically resembling morphea with a tuberculous background and indeterminate histology, suggestive of necrobiosis lipoidica, 737
- Wilkinson, W. Camac.**—Two cases of tuberculosis treated with tuberculin, 935
- Willcox, A.**—Lupus vulgaris with cutaneous horns, 1337
- Willcox, Sir William**—Cutaneous xanthomatosis associated with established diabetes mellitus, 526
- Williams, D.**—Retrobulbar neuritis, ? Devic's disease, 394
- Williams, E.**—Modified Mayo operation for proclivencia, 1282
- Williams, T. Pearce.**—Lipodystrophia progressiva, 1071
Influenzal meningitis, with complete recovery, 877
Megaduodenum (specimen), 875
- Wilson, C.**—Discussion on nutrition and its effects on infectious disease, 1052
- Wilson, D. S. P., and Lapage, C. P.**, Tumour of spinal cord in child aged 2½ years: specimen, 1185
- Wilson, Justina**—Discussion on short-wave therapy, 216
- Wilson, R.**—Three cases illustrating surgical treatment of bronchiectasis in childhood, 399
- Wilson, R. A., Torrey, M. A., and Johnson, K. S.**—The initiation of respiration in asphyxia neonatorum, 1461
- Wilson's disease** with Kayser-Fleischer ring, case of, 858
- Wingfield, A.**—Three cases of aortic aneurysm, 757
- Winsbury-White, H. P.**—Discussion on genito-urinary tuberculosis, 1442
Specimens from three cases of ureterocele, 1078
Two specimens of renal growth, 448
- Winterton, W. R.**—Adenomyoma malignum, 563
Fœtus amorphus (anideus), 564
- Wood, B.**—Discussion on effects of asphyxiating gases on the respiratory system, 1036
Discussion in treatment of pleural effusions, 846
- Woolf, A. E. M.**—Osteo-arthritis of right hip, treated with an extra-articular bone graft. Osteo-arthritis of the right knee, treated with auto-fat injection, 757
- Wolf, E.**—Hemispherical formations in Bowman's membrane, 701
? Sarcoma of choroid. ? Retinitis exudativa externa, 948
- Woods, Sir Robert S.**—Discussion on injuries of peripheral nerves, 870
- Workmen** using vibrating instruments, Raynaud's phenomenon in (J. H. Hunt), 171
- Wounds**, penetrating, nerve injuries due to, 868
- Wright, A. D.**—Discussion on urinary antiseptics, 514
Solitary plasma-celled myeloma of vertebral body, causing paraplegia, 931
Tonic spasm of arm: ? effect of encephalitis, 393
and **Feiling, A.**—Spina bifida occulta with nervous symptoms: relieved by operation, 574
- Wyllie, W. G. and Walter, W. G.** The electro-encephalogram in the diagnosis of cerebral pathology, 578
- Xanthomatosis**, cutaneous, associated with established diabetes mellitus, 526
nodular non-diabetic, with hypercholesterolemia and atypical histological features, 522
- X-ray** therapy, deep, effect of, in case of carcinoma of hypopharynx and cervical glands, 918
- Yates, A. L.**—Lichen planus involving the mouth, 499
- Young, J.**—Discussion on relative value of upper- and lower-segment Cæsarean operations, 562

case

sm,

ito-

078

563

ing

ns,

pip,

one

ee,

an's

iva

s of

id's

s

tics

eral

393

ith

on,

cro-

eral

ab-

nia

ma

018

th,

er-

ns,

VOL. XXX NO. 12

OCTOBER, 1937

MEDICAL LIBRARY

PROCEEDINGS
of the
ROYAL SOCIETY OF
MEDICINE



LONGMANS, GREEN & CO^L^{TD}

39, PATERNOSTER ROW, LONDON

NEW YORK · BOMBAY · CALCUTTA · MADRAS

All rights reserved



'VENTRON' Capsules

'Ventron' is a combination suitable for the treatment of many forms of primary and secondary anæmia and for use as a general hæmatinic and tonic in any form of debility, especially in patients recovering from operations or severe infections. It contains desiccated gastric tissue (Ventriculin) in concentrated form, together with the vitamin B complex, and iron and sodium citrate—a neutral soluble iron compound that is practically non-irritating to the gastro-intestinal tract and has a decided advantage over most other preparations.

'Ventron' is issued in hermetically-sealed capsules, which eliminate the taste and bulk associated with other methods of exhibiting desiccated gastric tissue.

Supplied in bottles of 50 capsules.

Parke, Davis & Company
50-54 Beak Street, London, W.1

Laboratories: Hounslow, Middlesex : Inc. U.S.A., Liability Ltd.

TEXTBOOKS

GLAISTER and BRASHE'S MEDICO-LEGAL ASPECTS OF THE RUXTON CASE. Crown 4to, 300 pp., with 172 illustrations. 22s. net; postage 6d.

(September, 1937)

"The Medico-Legal and other scientific aspects of a case without parallel in the annals of crime."

WHEELER and JACK'S HANDBOOK OF MEDICINE. Tenth Edition. Revised by Professor Henderson. 720 pp., 120s. 6d. net; postage 6d.

(August, 1937)

"As valuable now to the student and practitioner as it has ever been in its forty years of existence."

—The Lancet.

STEWART and DUNLOP'S CLINICAL CHEMISTRY IN PRACTICAL METACINE. Second Edition. Revised and enlarged. 384 pp. Illustrated. 20s. 6d. net; postage 6d.

New and thoroughly revised edition of this practical handbook. (Ready October, 1937)

CONYBEARE and CONTRIBUTORS A TEXTBOOK OF MEDICINE. Third Edition. 1050 pp. Illustrated. 21s. net; postage 7d.

(October, 1936)

"Will continue to occupy a foremost place among the textbooks on medicine of to-day."—Post-Graduate Medical Journal.

CATALOGUE FREE ON REQUEST

E. & S. LIVINGSTONE
16 and 17, Teviot Place, Edinburgh

PRIVATE PATIENTS.

LONDON COUNTY COUNCIL.

Accommodation for male patients (voluntary, temporary or certified) is provided in the Private Section of **CLAYBURY MENTAL HOSPITAL**, Woodford Bridge, Essex. Terms, exclusive clothing and special luxuries, 42s. a week for London cases, 49s. a week for others.

For particulars apply to the **MEDICAL SUPERINTENDENT** at the Hospital, or to the **CHIEF OFFICER**, Mental Hospitals Department, Shell-Mex House, Strand, W.C.2.

Suction
in
Surgery



The "CHIRON"

PORTABLE PEDAL ASPIRATING PUMP

clears the operation field of blood and secretions—A slight press of the foot being usually sufficient—It is noiseless in action. Under normal conditions a vacuum of 20 to 25 inches of mercury is easily obtainable.

Especially useful in:

Oral, Abdominal, Pelvic and Bladder Surgery, obviating the necessity of constant swabbing.

Full particulars on request.

MAYER & PHELPS Ltd.

Surgical Instrument Manufacturers
ESTABLISHED OVER 70 YEARS

CHIRON HOUSE,

39-61, NEW CAVENTISH ST., LONDON, W.1.

For the Injection Treatment of VARICOSE VEINS

'VIULES' QUININE AND URETHANE

QUININE and URETHANE has the advantage of being painless during injection. Quinine hydrochloride, B.P. has been used in the preparation of this product, and although less soluble than quinine bihydrochloride it has been found to be clinically much more effective in treating varicose veins.

Supplied in 2 c.c., 3 c.c., and 5 c.c. ampoules.
Single ampoules and boxes of 6 ampoules.
20 c.c. rubber-capped vials.

'VIULES' SODIUM SALICYLATE 30%

SODIUM SALICYLATE 30% is of particular value in the treatment of patients who have an idiosyncrasy to quinine, and is sometimes preferred when the veins are large.

Supplied in 2 c.c., 5 c.c., and 5 c.c. ampoules.
Single ampoules and boxes of 6 ampoules.

Literature sent on request

Wholesale and Export Department
Boots Pure Drug Company Ltd.
Nottingham

